A PROSPECTIVE OBSERVATIONAL STUDY COMPARING THE EFFECT OF ENDOTRACHEAL TUBE WITH SUBGLOTTIC SUCTION PORT(ETT SS) VS STANDARD ENDOTRACHEAL TUBE (ETT C) ON INCIDENCE OF VENTILATOR ASSOCIATED PNEUMONIA(VAP) IN PATIENTS ADMITTED TO INTENSIVE CARE UNIT.

Dissertation submitted in partial fulfillment of the requirement of

The Tamil Nadu Dr. M.G.R. Medical University for the M.D.

Branch XI (Anesthesiology) Examination to be held in April 2015

CERTIFICATE

This is to certify that

"A Prospective Observational Study comparing the effect of Endotracheal Tube with Subglottic Suction Port(ETT SS) vs standard Endotracheal tube (ETT C) on Incidence of Ventilator associated Pneumonia(VAP) in patients admitted to intensive care unit ."

*is a bonafide work of Dr. Sivakumar. G reg.no-*201320360 *in partial fulfillment of the requirements for the M.D. Anesthesiology examination (Branch XI) of The Tamil Nadu Dr. M.G.R Medical University to be held in April 2015.*

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A Prospective Observational Study comparing the effect of Endotracheal Tube with Subglottic Suction Port (ETT SS) Vs standard Endotracheal tube (ETT C) on Incidence of Ventilator-associated Pneumonia(VAP) in patients admitted to intensive care unit .
Dr. Sivakumar. G, Senior Resident, Anaesthesiology, Dr. Subramani. K, Surgical Intensive Care Unit, Dr. Nithin Abraham Raju, Surgical Intensive Care Unit, CMC, Vellore.

Ref: IRB Min No. 8999 [OBSERVE] dated 04.08.2014

Dear Dr. Sivakumar. G,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
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Ref: IRB Min No. 8999 [OBSERVE] dated 04.08.2014

Dear Dr. Sivakumar. G,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "A Prospective Observational Study comparing the effect of Endotracheal Tube with Subglottic Suction Port(ETT SS) vs standard Endotracheal tube (ETT C) on Incidence of Ventilator associated Pneumonia(VAP) in patients admitted to intensive care unit ." on August 4th 2014.

The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Sivakumar. G, Subramani. K, Nithin Abraham Raju.
3. Informed Consent Form (English, Tamil & Hindi)
4. Information Sheet (English, Tamil & Hindi)
5. No of documents 1-4

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We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

Fluid Grant Allocation:

A sum of 5,000/- INR (Rupees Five Thousand only) will be granted for 6 months.

Yours sincerely,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

NOT TO BE MINISTERED UNTO BUT TO MINISTER
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I sincerely thank all the staff members of Surgical ICU, A ICU and Medical Records Department, without them it would not have been possible to complete this Dissertation.

I shall be always grateful to my guide ***Dr. Subramani. K*** *who has been a mentor for many years now will remain one for many more years. Thanks to him for lending his precious time for this research and for his constant encouragement, calm attitude in critical times.*

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And finally I shall always remember ***my wife and son*** *for their help and support in needful times while pursuing this dissertation.*

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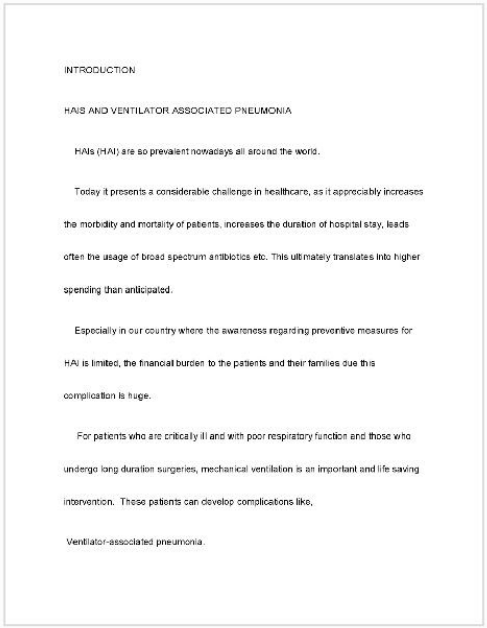

INTRODUCTION

HAIS AND VENTILATOR ASSOCIATED PNEUMONIA

HAIs (HAI) are so prevalent nowadays all around the world.

Today it presents a considerable challenge in healthcare, as it appreciably increases the morbidity and mortality of patients, increases the duration of hospital stay, leads often the usage of broad spectrum antibiotics etc. This ultimately translates into higher spending than anticipated.

Especially in our country where the awareness regarding preventive measures for HAI is limited, the financial burden to the patients and their families due this complication is huge.

For patients who are critically ill and with poor respiratory function and those who undergo long duration surgeries, mechanical ventilation is an important and life saving intervention. These patients can develop complications like,

Ventilator-associated pneumonia.

TITLE OF ABSTRACT:

"A prospective observational study comparing the effect of endotracheal tube with subglottic suction port (ETT SS) vs. standard endotracheal tube (ETT C) on incidence of Ventilator associated pneumonia (VAP) in patients admitted to intensive care unit."

DEPARTMENT: Dept. of Anaesthesia, Christian Medical College, Vellore, Tamil nadu.

NAME OF THE CANDIDATE: SIVAKUMAR. G

DEGREE AND SUBJECT: MD Anaesthesiology

GUIDE: SUBRAMANI. K

OBJECTIVE:

An observational study to compare the incidence of Ventilator Associated Pneumonia in patients intubated with standard E.T tube ETT C vs. ETT SS Subglottic suction drainage tube in ICU.

METHODS:

Adult patients admitted to intensive care unit (ICU) with duration of artificial respiration >48 hrs. were included in this study. The type of ET tube used for intubation was noted. Surveillance for Ventilator Associated Pneumonia in this study was in accordance with the latest "Surveillance for ventilator-associated events in the National Healthcare Safety Network (NHSN)" guidelines released in Jan 2014. Variables like Patient details, diagnosis, pre-existing illness, APACHE II, number of days on ventilator, number of days of ICU & hospital stay and hospital mortality were noted in both groups.

RESULTS:

In total 88 patients were enrolled in the study, 43 in ETT SS group and 45 in ETT C

group. The incidence of VAP in our ICU was 4.24 per 1000 ventilator days. The incidence of VAP was lower in ETT SS (0 %) compared with ETT C group (4.44%) though, were not statistically significant because of the small incidence. The overall incidence of VAE- Ventilator associated events

(VAC+IVAC+POSSIBLE VAP+PROBABLE VAP) when both groups combined

Was 16.94 per 1000 ventilator days. The incidence of VAE between the two groups were

similar as there were 5 (11.6 %) VAE in ETT SS group vs. 3 (6.6 %)

CONCLUSION:

The incidence of VAP in ICU showed a reduced trend with the use of ETT SS in comparison with

ETT C.

INTRODUCTION

HAIS AND VENTILATOR ASSOCIATED PNEUMONIA

HAIs (HAI) are so prevalent nowadays all around the world.

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Especially in our country where the awareness regarding preventive measures for HAI is limited, the financial burden to the patients and their families due this complication is huge.

For patients who are critically ill and with poor respiratory function and those who undergo long duration surgeries, mechanical ventilation is an important and life saving intervention. These patients can develop complications like,

- Ventilator-associated pneumonia.
- Septicemia
- Acute Respiratory Distress Syndrome.
- Barotrauma
- Pulmonary embolism,

- Pulmonary edema, etc.

The above mentioned statuses can lead to increased,

- Duration of mechanical ventilation,
- ICU and hospital stay
- Healthcare costs, and
- Risk of morbidity and mortality.

Among the complications mentioned earlier, Ventilator associated pneumonia or VAP is one of the common HAI, associated with increased morbidity and death in ICU s(1).

Studies have demonstrated that the risk of HAI in ICU ranges from 8% to 25%, with an incidence of 5 to 10 cases per 1000 ventilator-days (2,3).

VAP alone can result in requirement of

- broad spectrum antibiotic usage,
- prolongation of ventilatory days,
- increase in duration of ICU stay,
- increased duration of stay in hospital,
- increased mortality & morbidity and

- increase in cost of treatment 9.

Multiple preventive measures are used to prevent this complication; the current recommendations (6) are,

1. Head end elevation of the cot by 30-40 degrees,
2. Strict cuff pressure maintenance in the E.T. tube (20-25) cm H20
3. Oral hygiene
4. Circuit changes at regular intervals or when soiled with secretion ,
5. Using heated humidifiers and HMEs (heat and moisture exchanger) ,
6. Providing oral care with chlorhexidine and water-soluble mouth moisturizer ,
7. Use of specially designed E.T. tube for removing secretions,
8. Use of Closed- in-line suction,
9. Assessment for kinetic bed therapy
10. Employing sedation holiday
11. Appraisal of weaning readiness with spontaneous breathing trials whenever feasible
12. Stress related gastric ulcer prophylaxis and
13. DVT prevention strategies.

One of the postulated causes of ventilator associated pneumonia (VAP) is micro-

aspiration of subglottic secretions.

Among several factors, micro aspiration of these oral secretions, which pool in the laryngopharynx above the cuff of endotracheal tube leads to VAP.

Standard endotracheal tubes (ETT C) do not have an option to remove these secretions. But, newer endotracheal tubes with a dedicated suction port just above the cuff (ETT SS) are available these days.

This new design of endotracheal tube (ETT SS), which has facility to aspirate the subglottic secretions through an additional port intermittently or continuously.

Some studies have shown a reduction in Ventilator Associated Pneumonia when ETT SS was used . This has not been studied in our institution.

Some other earlier studies have not shown definitive benefit for the clearance of subglottic secretions in reducing the incidence of Ventilator Associated Pneumonia (2,7–13), therefore requiring further research to support this intervention.

In our study we hypothesize the use of ETT SS will decrease the incidence of Ventilator Associated Pneumonia.

In addition the surveillance in the past were less clear for Ventilator Associated Pneumonia as earlier definition(s) of Ventilator Associated Pneumonia was less objective with parameters like chest x-ray which is very subjective.

To make surveillance more objective, Centers for Disease Control and Prevention released a set of recommendations in January 2014.

This recommendation is based on objective, efficient, and possibly automatable criteria that will deliberately identify a wide range of conditions and complications happening in mechanically ventilated patients.

There are three definition levels within the ventilator associated event (VAE) algorithm: (14)

1) Ventilator Associated Condition (VAC);

2) Infection related Ventilator Associated Complication (IVAC); and

3) Possible and Probable Ventilator Associated Pneumonia.

The above definitions are described in detail later.

As a standard practice ETT SS is used for all intubations performed in our ICU. Patients intubated outside our ICU (who are subsequently transferred to our ICU for ventilation) for example in the Accident and Emergency Department, Operation Theaters etc are intubated with ETT C.

Therefore, we decided to do a research to find out whether the usage of ETT SS in our Intensive Care Units does impact the incidence of Ventilator Associated Pneumonia or not.

And also we decided to use the latest VAP surveillance algorithm released by CDC in January 2014 for our research.

AIM OF THE RESEARCH

AIM:

To compare the incidence of Ventilator Associated Pneumonia in patients intubated with standard E.T tube ETT C vs ETT SS ie. Subglottic suction drainage tube in the intensive care unit.

OBJECTIVES OF THE RESEARCH

OBJECTIVES OF THE RESEARCH:

1) To study the incidence of Ventilator Associated Pneumonia in both group of patients in general,

2) To study the incidence of Ventilator Associated Events in particular such as,

   a) Ventilator Associated Condition (VAC)

   b) Infection related Ventilator Associated Complication (IVAC)

   c) Possible Ventilator Associated Pneumonia and

   d) Probable Ventilator Associated Pneumonia.

3) To study the

   a) duration of mechanical ventilation ,

   b) duration of ICU stay and

   c) duration hospital stay in both the groups

4) To find the in hospital mortality in both groups of patients.

REVIEW OF LITERATURE

HAIS

World Health Organization defines HAI as,

"An infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility."(1)

HAIs like

- surgical site/wound infection,
- infection of urinary tract and
- respiratory infections.

are a major cause of morbidity and mortality not only in developed countries but also in developing countries like India.(1–3)

One of the highest prevalence of HAI happens in ICUs.(1)

Especially device related infections such as

- Ventilator-associated pneumonia ,

- Central venous catheter related infections and
- Catheter related urinary tract infections

pose a big threat to patient safety in the Intensive Care Unit .(2)

There are a few studies done till now estimating increased spending as a result of HAI or Hospital acquired infections in our country. In India, health insurance coverage among our population is said to be less than 15% or less. Health related payments are managed primarily out-of-pocket in our country and this sort of payment is comparatively among the highest in the world.(3)

Thus, nosocomial infections has serious implications on the Indian patient creating additional burden of costs and suffering.

So, the issue of HAI hospital acquired infections need to addressed comprehensively enabling an optimized and efficient health care planning, organisation and implementation.(1–3)

In some studies, hospital-acquired infection HAI rates is about 1% in the developed countries and in the other extreme more than 40% in developing countries in certain parts of Asia, Latin America and Africa.(3)

The above mentioned data reflects the huge burden posed by HAIs in poorer countries where the economic reserve of an individual patient as well as of these governments as a whole is limited and unequally distributed.(3)

In our country for example where one sixth of the world's population reside, the additional burden of costs attributable to these infections has serious inferences such as emotional stress and disabling conditions that reduces the quality of life..

Therefore, warranting strict adherence to known HAI preventive measures and constant need for continued research, surveillance and accountability.

In-spite of huge (often unequal) progress in public health-care in our country, infections continue in hospitalised patients even putting healthcare personnel at risk of infection.(2,3)

The main factors that promote infection among hospitalised patients are(1,2),

- Extremes of age— neonates, infants, and elderly people,
- lesser immunity among patients,
- Length of hospital stay
- Catheters in situ and invasive medical procedures,
- invasive techniques and interventions creating potential routes of infection,
- Unjustified antibiotic usage and the spread of drug-resistant pathogens ,

- Use of antacids in ulcer prevention,
- Mechanical ventilation,
- Use of total parenteral nutrition,
- lack and of strict adherence to infection control practices .

PREVENTIVE MEASURES FOR NOSOCOMIAL INFECTIONS

The folowing are the recommended preventive measures for HAI,

1) Hand washing(4):

- as often as possible especially before and after touching patients and their associated equipments , articles etc.
- use of alcoholic hand spray because it acts rapidly, more efficient and minimal time commitment, allows easy and complete compliance.
- removing jewelery before washing hands.
- Continuous monitoring and education to encourage hand washing.

2) Cleaning stethoscopes, ultrasound probes, monitoring aids, oxygen masks etc. between patients and usage of barrier covers.

3)Gloves(4): as an accessory to hand washing

4)In case of invasive line insertions(4)s:

- strict aseptic precaution and use of alcoholic chlorhexidine or 70% isopropyl alcohol for at least 30 seconds and should be allowed to dry before inserting the cannula.
- changing i.v. sets every 3 days.
- use of a clear, adhesive, polyurethane dressings (Tegaderm) which are more permeable instead of standard dressing to reduce moisture accumulation and

infection rates.(4)

5) Strict adherence Ventilator Associated Pneumonia bundle in ventilated patients for ventilator associated pneumonia prophylaxis. (5,6)

6)Use of mask, gown even-though the evidence is conflicting should be at least done for invasive procedures.

7) Avoidance of white coat and use of disposable aprons for close contact examinations, dressings etc.(4)

8)Continued surveillance pro-grammes for accountability of infection control practices and its effectiveness.(7)

8)Continued education and creating awareness regarding nosocomial infections and preventive strategies among health care personnel and the hospital population.(2,4,7)

Despite the awareness and the various preventive measures nosocomial infections continue to haunt our hospitals especially our ICUs. It is the most common nosocomial infection in patients who are mechanically ventilated in the critical care units (ICUs). (8,9)

Also, VAP is the 2nd commonest HAI in critical care units contributing to about 50 % of all cases of hospital-acquired pneumonia.(8,9)

Therefore, we decided to do a research to find out the incidence ofVAP- ventilator

associated pneumonia, the commonly acquired nosocomial infection in our ICU.

By the end of this research we will know whether the Ventilator Associated Pneumonia bundle plus the use of specially designed endotracheal tubes makes a significant impact in its prevention.

VENTILATOR ASSOCIATED PNEUMONIA (VAP)

INTRODUCTION:

As we come across the literature, the definition for Ventilator Associated Pneumonia or VAP keeps changing over time but controversy does not, and the definition given below will be one of the most acceptable one.

"Ventilator Associated Pneumonia (VAP) is defined as pneumonia occurring in a patient within 48-72 hours or more after intubation with an invasive airway (endotracheal tube or tracheotomy tube) and which was not present earlier".

Which is defined by the presence of

- a new or progressive patchy infiltrate on chest radiography,
- signs of systemic infection like hypothermia or febrility,
- abnormal WBC count Leucocytosis > 12000WCC/uL or leucopenia <4000 WCC /uL,
- changes in color/character of sputum or endo-tracheal aspirate , and
- detection of an infective agent by microbiology .

It is the commonest nosocomial infection in patients who are mechanically ventilated in the critical care units (ICUs).

As we said earlier, VAP is the 2nd commonest nosocomial infection in the critical care unit contributing to about half of all cases of hospital-acquired infections.

Especially in mechanically ventilated patients incidence ventilator associated pneumonia is is about 9–27 %, with the higher risk during early period of hospitalization.(8,9)

Considerable investigation efforts were made in the last decade in the field of the of ventilator-associated pneumonia and its management. Previous scrutinies have provided important knowledge regarding the histology and bacteriology concerning ventilator associated pneumonia ,which is important to later research.

Various earlier epidemiological studies have established new concepts for empirical initial antibiotic treatment for ventilator associated pneumonia that are expected to improve clinical outcomes. Over the years, crucial developments have been made regarding ventilator associated pneumonia prevention. (10)

Having said that, most of the issues concerning the diagnosis and treatment of ventilator associated pneumonia remains unsettled and contention exists till date.

There is no consensus in diagnostic evaluation of ventilator-associated pneumonia and that partly explains why incidence of ventilator associated pneumonia rates vary widely in different studies. (7–10)

And it was apparent we came across earlier studies, they place the risk of death for Ventilator Associated Pneumonia at between 5–50 % almost (doubling mortality in some studies). But this proportion is variable and depends to a great extent on the underlying medical ill health.(8–10)

In recent years, the attributable risk of mortality has decreased to about (9–13 %) mainly because of implementation of Ventilator Associated Pneumonia preventive strategies.(8,9,11)

In our hospital which is a tertiary care referral center we continue to face the problem of ventilator associated pneumonia and despite having a hospital infection control committee (HICC) which surveys the annual incidence of all hospital acquired infection HAIs.

According to hospital infection control committee's (HICC) recent surveillance the incidence of VAP in all our ICUs put together is about 40% in the previous year.

In the coming sections we shall discuss in detail about,

1. *THE ETIOLOGY OF VENTILATOR ASSOCIATED PNEUMONIA,*
2. *THE PATHOGENESIS OF VENTILATOR ASSOCIATED PNEUMONIA ,*
3. *RECOMMENDED PREVENTIVE STRATEGIES AND THE SUPPORTING EVIDENCE,*
4. *RECENT UPDATES IN THE SURVIELLANCE OF VENTILATOR ASSOCIATED PNEUMONIA AND ITS PRACTICAL IMPLICATIONS,*
5. *THE ROLE OF SUBGLOTTIC SECRETION CLEARANCE IN*

PREVENTION OF VENTILATOR ASSOCIATED PNEUMONIA,

6. *LABOROTARY DIAGNOSTIC MODALITIES AND*
7. *CHALLENGES IN ANTIBIOTIC TREATMENT OF VENTILATOR-ASSOCIATED PNEUMONIA.*

ETIOLOGY OF VENTILATOR ASSOCIATED PNEUMONIA

In majority of the reports we came across the three leading etiologies for ventilator associated pneumonia are,(8,10)

- Gram negative bacilli,
- Pseudomonas aeruginosa and
- Staphylococcus aureus .

But, it is important to know that in early-onset ventilator associated pneumonia the causative organisms can be so called community bacteriae such as

- Streptococcus pneumoniae
- MSSA-methicillin sensitive S. aureus
- Haemophilus influenzae and
- Gramnegative enteric bacilli,

On the other hand in late-onset VAP the causative organisms are,

methicillin-resistant staphylococcus aureus (MRSA),

- Pseudomonas aeruginosa,
- Acinetobacter baumannii and
- Stenotrophomonas maltophilia.

Majority of these organisms are possibly drug-resistant and are found to be associated with increased morbidity and mortality.

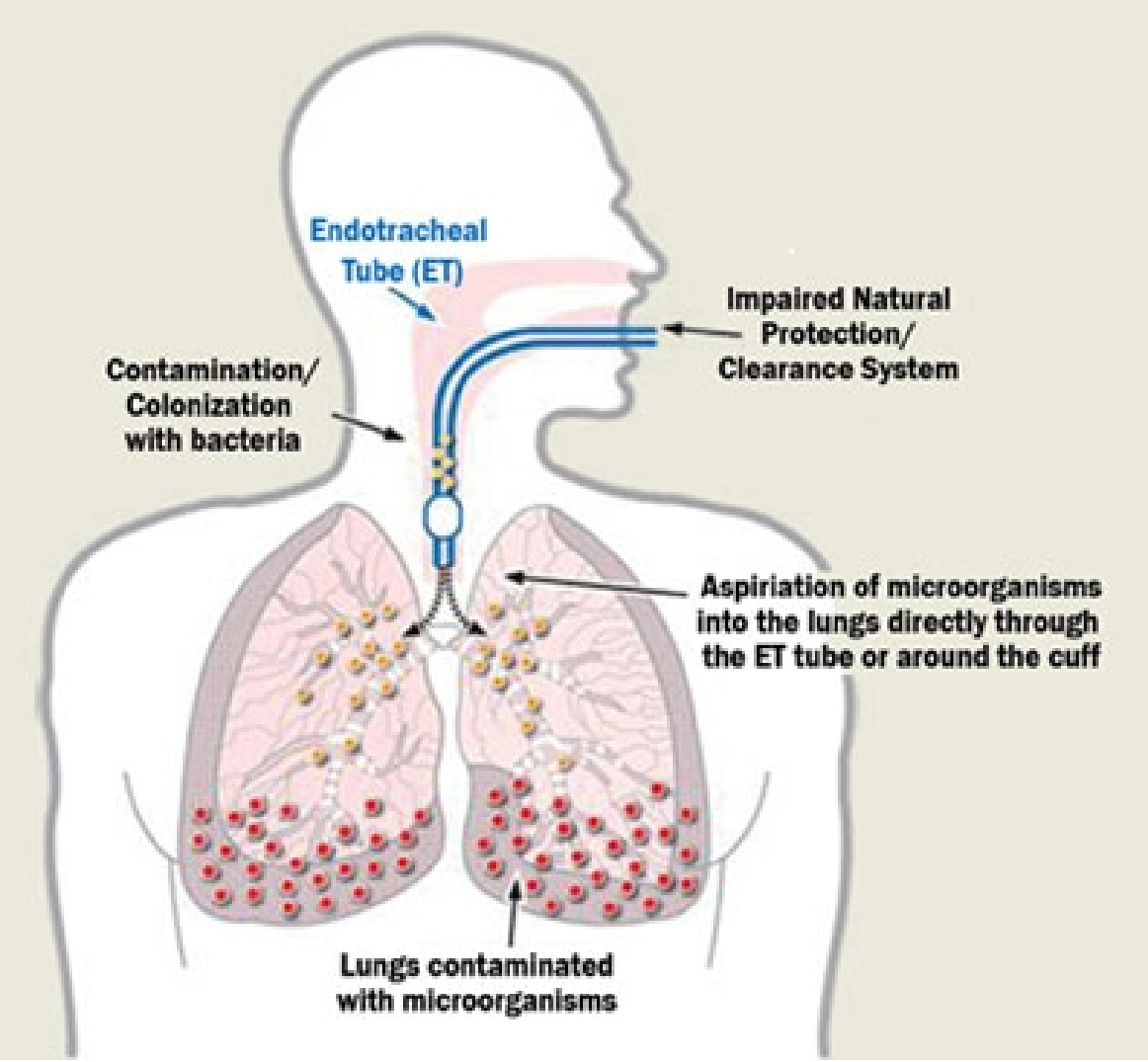
We also note that an important unresolved issue in VAP is the definition of early and late onset VAP. Even though it remains unclear whether it concerns the number of hospital days or to the number of days after intubation, it is usually the first 5 -7 days which separate early onset and late onset VAP.(10)

The etiological agents varies from patient to patient and may also differ with intensive care units, hospitals and countries and most importantly vary in a given ICU over the period of time. Thus, reported differences in VAP etiology can frequently be explained by

- local specificities.
- The primary illness,
- Associated co-morbid conditions,
- Length of hospital stay and intubation,
- Previous exposure to antibiotics,
- Effectiveness or the lack of effective VAP preventive strategies and
- The selection of the initial empiric antimicrobial treatment and susceptibility patterns of the pathogens.(8,10)

THE PATHOGENESIS
OF
VENTILATOR ASSOCIATED PNEUMONIA

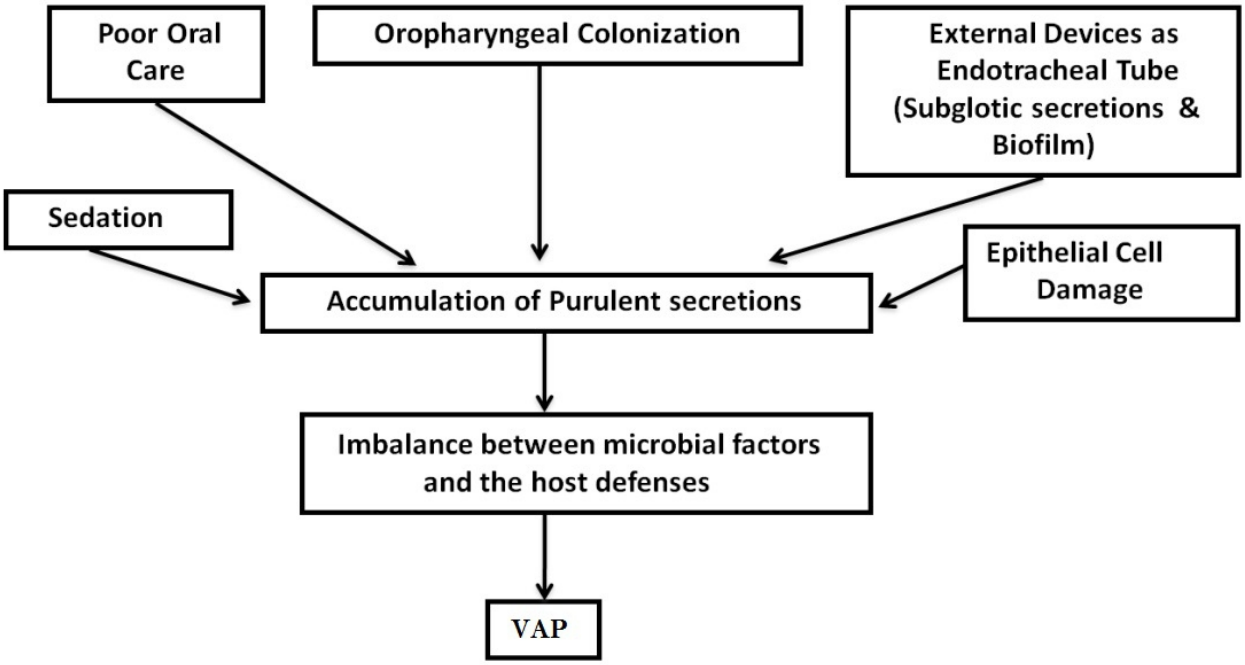
Figure showing the "Path to Ventilator-Associated Pneumonia"



As shown in pic above in the ventilated and critically ill patients, production of saliva decreases and the subsequent environment promotes bacterial colonization in the mouth and oropharyngeal secretions, and can rapidly cause the development of pneumonia.

PATHOLOGY OF VENTILATOR ASSOCIATED PNEUMONIA.

FLOW CHART DEPICTING THE PATHOGENESIS OF VAP:



THE INTERPLAY BETWEEN INVASIVE DEVICES AND RISK FACTORS.

The following three factors that are critical in pathogenesis of ventilator-associated pneumonia.

1. The colonization of the oropharynx with pathogenic microorganisms in intubated patients,

2. Micro-aspiration of these secretions filled with pathogens from oropharynx into lower respiratory tract past (around) the endotracheal tube cuff.

3.Compromise of the host defense mechanism (in patients who are critically ill).(12)

So, it is a the complex interplay between

- The endotracheal tube and other invasive devices eg. naso gastric tube.
- The presence of risk factors (underlying disease, previous surgery and antibiotic exposure, reintubation etc).
- The virulence of the invasive pathogen and
- The patient's immunity .

which mostly determines the development of ventilator associated pneumonia . (8)

ROLE OF ENDOTRACHEAL TUBE IN PATHOGENESIS OF VAP

By far the most obvious risk factor for VAP is the of endotracheal tube's presence of E. T.tube because of the following,

- It bypasses the normal mechanical factors preventing aspirations such as the cough reflex of glottis and larynx.
- It leads to is disruption of competent anatomical barriers allowing a straightforward communication between the supra-glottic space and the lower respiratory tract.
- The cuff of the endo-tracheal tube can only prevent gross aspiration not micro aspiration.
- If they become contaminated with bacteria from patients secretions even the contamination of ventilator circuit, heat moist exchangers and respiratory therapy equipment can lead to the development of ventilator-associated pneumonia.
- Trickling of pooled secretions around the ETT cuff.
- The perfect seal with the cuff is not possible due to, the formation of folds along the tracheal surface, frequent movement, inadequate inflation etc.
- The cuff also creates a mechanical obstacle to mucus clearance and impairs

muco-ciliary function.(13)

- The micro-aspiration can occur during intubation itself.
- Consequentially the endotracheal tube's presence and endo-tracheal suctioning can damage the tracheal mucosa facilitating tracheal colonization by pathogens.

BACTERIAL BIOFILM COATING ON ENDOTRACHEAL TUBE AND ITS IMPLICATIONS

Bacterial bio-film on the surface of endo-tracheal tubes has been observed universally in mechanically ventilated patients.

Evidence from recent data suggests a good relationship between microbial findings in the bio-film and bacterial colonization of the airway. The potential implication of bio-film in the pathological process of VAP is evident by the presence same microorganisms in the bio-film and the ones causing ventilator-associated pneumonia.(14)

Formation bio-film, as explained earlier by the pathogens on endotracheal tube's surface not only protects them from antibiotic and host defenses, these pathogens can dislodge during suctioning and the small fragments of glycocalyx can reach lower

respiratory tract carrying bacteria with them.

INVASIVE VS NON-INVASIVE VENTILATION IN PATHOGENESIS VAP

The muco-ciliary clearance of secretions is impaired in intubated patients and the mucus flow is gravity dependent in the airways.

Also anatomic structures like stomach, sinuses, naso-pharynx and oropharynx can act as reservoir for pathogenic material and their normal flora can be replaced by more virulent strains and this pathogen rich material is continuously pushed forward by the positive pressure ventilation.

Evidence also suggests that reintubation following extubation increases ventilator associated pneumonia rates and the use of non-invasive ventilation has been found to significantly reduce ventilator-associated pneumonia rates.(8,12)

ASSOCIATION OF ENTRAL NUTRITION AND VENTILATIOR ASSOCIATED PNEUMONIA

The “gastro-pulmonary hypothesis” postulates that, as stomach becomes

colonized with gram-negative bacterium in critically ill, it has a strong association with the development of ventilator associated pneumonia because, they are the most common organisms isolated from sputum of patients with ventilator associated pneumonia. This theory suggests a retrograde migration and colonisation of oropharynx from the gastrointestinal tract which in turn gets colonized by pathogenic microorganisms endogenously (contaminated liquid injected into a naso-gastric tube), or endogenously (duodeno-gastric reflux).And, subsequent sustained micro aspiration of this contaminated secretions from oropharynx or stomach, pooled above around the endotracheal tube's cuff ultimately leads to infection of the lower respiratory tract (15). There is evidence suggesting that a gastric pH of 3.5 plays a role in prevention of bacterial colonization which maintained in fasting conditions and a pH 4.0 is associated with significant bacterial colonization of stomach and its content in clinically significant proportions, resulting in increased incidence of nosocomial pneumonia.

But in Critically-ill patients especially who are ventilated and coagulopathic, stress-related gastro-intestinal bleeding results in higher mortality, compared to patients without evidence of bleeding so, warranting stress ulcer prophylaxis.(15), which increases gastric pH.

Enteral feeding especially continuous feeding through naso gastric tube increases gastric pH and may,tends to increase gastric residual volumes. Gastric residual volume is one of the risk factors for tracheo-bronchial aspiration by patients on ventilators but,

results of a recent systematic review is inconclusive.(16).

But, early enteral nutrition has got its advantages, as it reduces the hospital mortality. If initiated within 48 hours of mechanical ventilation, enteral nutrition in critically ill has shown to reduce mortality. This is especially beneficial in the sickest patients (hemodynamically unstable, with multiple vasopressors support) and there was no evidence of harm due to initiation of early enteral nutrition.(17)

ALTERED IMMUNOLOGY IN CRITICALLY ILL AND ITS ASSOCIATION WITH VAP

In patients who are critically ill pathogenic microorganism replaces the normal oropharyngeal flora due to cross infection from other patients and medical personnel, contaminated equipments (airway devices, ventilator circuits etc.)

Recent research in immunology shows in critically ill patients with septicemia and trauma, even prior to the emergence of nosocomial infection they can have ineffective phagocytosis and may act as functionally immune-suppressed. Due to their apoptotic loss of host cells adaptive immune system several days after admission in to ICU they are at a greater risk of developing ventilator associated pneumonia.(8,12,18,19)

This effect is attributed to the ineffective or impaired neutrophil phagocytic

activity due to detrimental actions of the anaphylatoxin C5a. Acquisition of nosocomial infections is attributed to a combined of T-cells monocytes and neutrophils dysfunction in recent research.

Researchers also suggested that infections in critically ill in contrast to healthy controls can be predicted by elevation of v regulatory T-cells, CD88 expression-neutrophil dysfunction and monocyte HLA-DR expression-monocytedeactivation(8,18,19)

PREVENTION OF VENTILATOR ASSOCIATED PNEUMONIA

RECOMMENDED VAP PREVENTION STRATEGIES AND THE SUPPORTING EVIDENCE

Current recommendations for adult intensive care unit patients for prevention of ventilator-associated pneumonia - ventilator associated pneumonia bundle interventions are as follows (2),

Head end elevation of the cot by 30-40 degrees,

Strict cuff pressure maintenance in the E.T. tube (20-25) cm H20

Oral hygiene

Circuit changes at regular intervals or when soiled with secretion ,

Using heated humidifiers and HMEs (heat and moisture exchanger) ,

Providing oral care with chlorhexidine and water-soluble mouth moisturizer ,

Use of specially designed E.T. tube for removing secretions,

Use of Closed- in-line suction to remove tracheal secretions,

Assessment for kinetic bed therapy

Employing sedation holiday

Appraisal of weaning readiness with spontaneous breathing trials whenever feasible

Stress related gastric ulcer prophylaxis and

DVT prevention strategies.

The evidence behind these preventive strategies are discussed in detail in coming sections.

A) Nursing and Respiratory Care

Head-end Elevation of the Bed

In the absence of contraindications, all ventilated patients should be nursed with head end of the bed elevated at an angle of 30-40 degrees. Incidence of ventilator associated pneumonia due to aspiration was found to be higher in patients who were not nursed in the head up position. Head end elevation of the bed for any degree less than 30 was not found to be beneficial in reducing risk of aspiration. Patients receiving entral tube feeds were found to be at higher risk for aspiration leading to ventilator associated pneumonia.

Maintaining Endotracheal tube's Cuff Pressure

Maintenance of endotracheal tube's cuff pressure between 20-25 cm H_2O.

Ventilator associated pneumonia incidence was found to be reduced in patients

whom cuff pressure was maintained above 20 cm H2o.

During mechanical ventilation endotracheal tube cuff pressure decreases spontaneously and can result in aspiration of pooled oropharyngeal secretions into the lower respiratory tract thereby increasing the risk of ventilator-associated pneumonia.

The Centers for Disease Control and Prevention does not recommend maintenance of endotracheal cuff pressures above 20 cm of h2o.

Circuit Change

The centers for disease control and prevention recommends changing of ventilator circuit only when visibly soiled, as frequent replacement of ventilator circuits did not reduce the incidence of ventilator associated pneumonia.

Heated Humidifiers, and Heat and Moisture Exchangers

Due to lack of evidence supporting the use of heat and moisture exchangers and heated humidifiers, The Centers for Disease Control and Prevention does not recommend their use as. studies failed to demonstrate a significant reduction in the incidence of ventilator associated pneumonia when either heated humidifiers or heat

and moisture exchangers were used.

The Centers for Disease Control and Prevention recommends that heat and moisture exchangers should be changed every 48 hours or on visible soiling and/or on evidence of mechanical malfunction.

Some authors have also proven an absence of adverse effects, with regard to either technical or clinical ventilator performance, even if the heat and moisture exchangers were not changed up to 120 hours.

Also, there is no evidence supporting that the frequent changes in heat and moist exchangers reduces the incidence of ventilator-associated pneumonia or endo-tracheal tube occlusion (2).

Oral Care

Oral decontamination with 2% chlorhexidine solution was evaluated in an earlier randomized controlled trial and a meta-analysis for the prevention of ventilator-associated pneumonia in comparison with normal saline solution.

Although using chlorhexidine mouth wash statistically reduced the incidence of ventilator-associated pneumonia per 1,000 ventilator days there no was difference in the incidence of gram negative oropharyngeal colonization and overall mortality.

Patients in the chlorhexidine group also reported a higher incidence of oral mucosal irritation which restricted the number of times oral care was administered.

Secretion Removal with Specially Designed Endotracheal Tubes

Several authors reported reduced rates of early onset ventilator associated pneumonia when specially designed endotracheal tubes capable of continuous aspiration of subglottic secretions were used. Hence the American Thoracic Society document recommends the use of specially designed endotracheal tubes capable of providing continuous suctioning of subglottic suction (3). The use of continuous subglottic secretions was found to cause mucosal injury by some observers.

Routine change of standard endotracheal tube to an endotracheal tube with a subglottic suction lumen is not recommended due to the risk of the aspiration during the change.

The Centers for Disease Control and Prevention recommends,

Use of specially designed endotracheal tube with a dorsal lumen proximal to the endotracheal cuff for the removal of pooled secretionby suctioning.

Ensure clearance of secretions proximal to the endotracheal tube cuff prior to

deflating the ETT cuff or changing the tube for any reason.

Patients expected to require more than 72 hours of mechanical ventilation, the use of endotracheal tube with special port for removal of subglottic secretions removal port, was found to reduce ventilator-associated pneumonia and duration of mechanical ventilation.

The working group of the centeres for disease control and prevention recommends use of these special endo-tracheal tubes in the case of a hospital wide practice and to appropriately determine its use patients who are expected to require prolonged mechanical ventilation. As patients requiring emergency intubation fall into this category often, these special tubes should be available in the casualty or ED and other areas where emergency intubations for are performed

Closed, In-Line Suctioning

The working group of The Centers for Disease Control and Prevention does not recommend the use closed in-line suctioning, in the protocol for prevention of ventilator associated pneumonia.

An earlier study observed, the use of in-line suctioning within 3 days, Significantly enhanced microbial growth within the lower respiratory tract, Normal saline instilled with endotracheal suctioning lead to dispersion of microorganisms into the lower respiratory tract. But, exposure of hospital personnel to infected respiratory

secretions was significantly decreased with closed systems.

So, *The Centers for Disease Control and Prevention does not make any preferential recommendation for the use of either single-use open suction system or multi-use closed suction system*. This is because, researchers could not demonstrate a decrease in the incidence of ventilator-associated pneumonia s with either systems.

A meta-analysis of 15 randomized trials comparing closed suction system to open suction system, failed to demonstrate any significant difference in incidence of ventilator-associated pneumonia and mortality between both the groups.

Kinetic Bed Therapy

The use of Kinetic bed therapy (continuous lateral rotation) reduced the incidence of VAP, in a prospective, randomized, multicenter study in 2004 (4) .

However, as kinetic bed therapy significantly decreased incidence of ventilator-associated pneumonia and lobar atelectasis, it did not offer any benefit with regard to duration of mechanical ventilation or mortality.

Hence there is *no strong recommendation for the routine of kinetic bed therapy*, as it requires a special bed that may not be available at all intensive care units.

Sedation Reduction

Use of regular spontaneous breathing trials, i.e. testing patient's ability to sustain

adequate ventilation, oxygenation and breathing comfort without ventilatory support, has been shown to significantly reduce duration of mechanical ventilation for acute respiratory failure.

Daily cessation of continuous infusions of sedative medications, after the second day of intubation was found to decreases the duration of mechanical ventilation and the need for diagnostic testing to evaluate impaired mental status that occurs after intensive care admission.

Use of sedation algorithms to frequently adjust sedative and analgesics doses and maintaining wakefulness was also shown to reduce number of ventilator days [C].

individualisation and modification of recommendations, to each intensive care unit is recommended.

- Essential sedation reduction elements include,
- Use of sedation scales for regular patient assessment,
- Cessation of sedation daily or hourly dose reduction in patients who are over-sedated,
- Opiates should be used as an adjunct for pain and
- Use of bolus dose to achieve desired level of sedation to be considered prior increasing the infusion rates.

The contraindications to sedative cessation include,

- Neuromuscular paralysis,
- Intense respiratory failure
- Withdrawal of life support .

Weaning Readiness

Use of Brief weaning trials daily (or more frequently), allowing early assessment of patients' ability to sustain breathing comfort, ventilation, oxygenation and hemodynamic stability are recommended.

Use of brief weaning trials was found to reduce number of days of mechanical ventilation significantly.

The patient's tolerance and physiological response to 30-60 minutes of unsupported (e.g., continuous positive airway pressure or T-piece) or minimally supported breathing (e.g., with pressure support of 7 cm H_2O) can be done by respiratory therapist or nurse-driven protocols, and can be communicated to physicians.

Weaning trial results should be incorporated only after the patient's level of consciousness, airway stability, illness course and hemodynamic status, are

considered.

The weaning trial can be temporarily postponed in the presence of:

- Raised Increased intracranial tension,
- Severe respiratory failure such as FiO_2 requirement greater than 50%,
- PEEP or positive end-expiratory pressure greater than or equal to eight,,
- Whenever prone position is used,
- In case of airway related problems or hemo-dynamic instability ,
- Whenever neuromuscular blockade is used,
- Apnea and
- Expected life support removal..

B) Medications

Stress Ulcer Prophylaxis

The Centers for Disease Control and Prevention does not make any recommendation for the preferential use of sucralfate, H2-antagonists, and/or antacids for stress-bleeding prophylaxis in patients receiving mechanical ventilation.

In a randomized clinical controlled study on 52 patients in an intensive care unit comparing ranitidine vs sucralfate for stress ulcer prophylaxis demonstrated that

there was no difference in the incidence of gastrointestinal bleeding between the ranitidine and sucralfate groups, but was higher in the control group.

In the ranitidine group the mean gastric pH was higher significantly .

In the ranitidine group the frequency of positive cultures with gram-negative bacteriae was found to be higher than the sucralfate group (75% compared to 33% with sucralfate).

In all three groups(i.e. ranitidine, sucralfate and control groups) the frequency of

positive growth in the broncho alveolar lavage culture was similar (5) .

Considering the available evidence discontinuation of stress ulcer prophylaxis for the patient should be considered ,

- Once they are extubated,
- When patient is transferred out of the intensive care unit and there is no significant gastrointestinal bleeding,
- In the absence of spinal cord and brain trauma,
- Patients getting enteral nutrition,
- Patient not on a high-dose steroids therapy and/ is not on any outpatient medication.

Venous Thromboembolism Prevention:

For most patients in the intensive care unit or those with risk factors for development of venous thromboembolism, venous thromboembolism prophylaxis is recommended.

Recent study, reviewing thromboembolism prevention for a variety of clinical conditions found out, most patients in the hospital have one or many risk factors for developing venous thromboembolism. Thromboprophylaxis should be used based on

solid principles and scientific evidence, as cumulative risk factors are present in most patients.

A strong correlation exists between asymptomatic deep venous thrombosis and later development of venous thromboembolism.

The prophylaxis for symptomatic deep venous thrombosis and pulmonary em-bolus should be a top priority as these complications are associated with increased mortality, increased costs and long-term complications.

Pneumatic compression devices increase venous outflow and/or reduce stasis within the leg veins therefore, should be considered for all patients who are at high risk for bleeding.

Even though these devices have been shown to decrease the risk of DVT but not to reduce mortality or pulmonary embolism.

These devices are acceptable for use in patients at increased risk for bleeding or can be used in addition with anticoagulant therapy.

It is recommended that all patients should be assessed for their risk of venous thromboembolism on admission to a critical care unit and accordingly, should receive thromboprophylaxis.

Although critically-ill patients are at a high risk for developing deep vein thrombosis and pulmonary embolism, are also at the risk for bleeding, thrombocytopenia coagulopathy and renal impairment.

So, different therapies for thromboprophylaxis might be appropriate, including combination of an anticoagulant medication (heparin s or fondaparinux) and intermittent compression devices at different times.

The so called the VAP bundle interventions discussed above and the preventive practices for all hospital acquired infections are strictly followed in our ICU. Also awareness among the healthcare personnel in our hospital in general and our ICU in particular is created through continuous education pro-grammes.

RECENT UPDATES IN THE SURVIELLANCE OF VENTILATOR ASSOCIATED PNEUMONIA AND ITS PRACTICAL IMPLICATIONS

The very definition and the diagnostic criteria for ventilator-associated pneumonia or VAP kept on evolving and changing since the time its been first recognised and continue to change every passing year.

For example,

The CDC Centers for Disease Control and Prevention defined ventilator-associated pneumonia (VAP) in 2002, as

“A new or progressive and persistent radio graphic abnormality developing in a patient on mechanical ventilation or within 2 days of mechanical ventilation, who must also demonstrate: one or more systemic signs (pyrexia, leucopenia or leucocytosis, or altered mental status in those >70 years of age) and selected pulmonary criteria (eg, change in respiratory secretions, new onset of cough, dyspnea, crepitations, bronchial breath sounds, or worsening oxygenation).

And with some additional criteria for VAP in immuno-compromised patients was also released then.

This above definition of ventilator-associated pneumonia could not be specifically used for surveillance purpose as it had been found to be neither sensitive nor specific.

The chest radiograph which was integral part of that definition, always had its pitfalls, when it comes to diagnosing ventilator-associated pneumonia because, haziness in a chest radiograph especially in a portable film could be due to various conditions like

pneumonia, atelectasis, pleural effusion or pulmonary edema and therefore making it unreliable in the diagnosis of ventilator-associated pneumonia alone.

The most accurate radio-graphic signs for ventilator-associated pneumonia were air broncho-gram and volume loss (not haziness) in suspected patients, which had a diagnostic accuracy of 64% and was proven in an earlier autopsy study (20). But, this investigation is subject to observer variability.

The given clinical features are every bit fallible for VAP surveillance purpose also proven in an earlier study as the sensitivity and specificity was around 69%-75% only (i.e. a radio-graphic opacity and 2 of 3 signs of infection such as pyrexia, leucocytosis, and mucopurulent sputum)(21)

Also, it was difficult to differentiate between colonization and infection with microbiological evidence as in various studies, about 22% of 95 intensive care unit patients became colonized, within 24 hours of intubation (22–24). Moreover, another issue is that, not all the laboratories report quantitative culture.

To makethe surveillance of VAP more objective, as the earlier definition of VAP was less objective with parameters like chest x-ray which is very subjective, the CDC – Centers for Diagnostic Control established a task force in 2011to develop new a surveillance strategy that can be put into practice by the NHSN or National Healthcare Safety Network of USA and therefore a new set of surveillance recommendations are released in January 2014. This recommendation is based on non subjective, efficient,

and possibly automatable criteria that will deliberately denote a wide range of conditions and complications which occur in ventilated patients in adult critical care units.

Thus a new collection of conditions, ventilator-associated events or VAE was coined, collection all the states that consequence a significant and continuous impairment in oxygenation in mechanically ventilated adult patients. It is now defined in patients ventilated for more than 2 days, *as a more than 20% addition in the daily minimum fraction of inspired oxygen or an addition of at least3 cm H2O in the daily minimum PEEP to hold up oxygenation*.

VAE definition may be fulfilled by both infectious conditions and noninfectious conditions. The definition VAE is three tiered, as follows:

Tier 1: **ventilator-associated condition (VAC)** after a 2 day period improving oxygenation or status quo the patient develops hypoxemia for a sustained period of more than 48 hours 0r 2 days irrespective of cause of hypoxemia.

Tier 2: **infection-related ventilator-associated complication (IVAC)** —in addition to VAC -hypoxemia develops along with picture of generalized infection or inflammation, and antibiotics are given for at-least four days.

Tier 3: **probable or possible ventilator-associated pneumonia (VAP)** —In patients with IVAC extra lab-evidence of abnormal WBC count, presence of neutrophils in respiratory secretion specimen of bankable quality, or (=possible VAP)/and (=probable VAP), presence of respiratory microorganisms on quantitative cultures,

Additional criteria are also given for use in meeting the possible VAP or probable VAP definitions.(25)

The Centers for Disease Control with the initial users feedback has made many modifications of the definitions in VAE surveillance algorithm which was utilised by the NHSN such as,

In some mechanically ventilated patients, PEEP is not used initially due to associated conditions for example, hypo-tension or, raised intracranial pressure and during spontaneous breathing trials, sometimes PEEP is reduced for short duration. But PEEP may be put back or increased when these conditions revert and the subsequent increase in PEEP will represent VAC in accordant to the new definition. So, these situations should be taken into account before recording the event.

E.g. if a patient is receives gentamycin for preexisting urinary tract infection, it shouldn't confused with respiratory tract infection treatment , this issue is addressed by limiting the qualifying list of antibiotics used in treatment of ventilator associated infection than those used for other infective conditions.

To make sputum examination reporting less rigorous laboratories – some labs may report counts of neutrophils and/or squamous epithelial cells in respiratory secretion specimen using various quantification outsets than recommended in the new algorithm.

Interventions like increasing the Fio2 or increasing PEEP level for comfort care in case of terminally ill shall not be defined as a VAC.

Above mentioned and many such doubts, clarification and problems in special situations are answered by NSHN in a new release and it is available in their website. **“http://www.cdc.gov/nhsn/pdfs/pscManual/10-VAE_FINAL.pdf “**

TIER 1: VENTILATOR-ASSOCIATED CONDITION (VAC)

Patient has a baseline period of stability or improvement on the ventilator, defined by ≥ 2 calendar days of stable or decreasing daily minimum* FiO2 or PEEP values. The baseline period is defined as the 2 calendar days immediately preceding the first day of increased daily minimum PEEP or FiO2.

**Daily minimum defined by lowest value of FiO2 or PEEP during a calendar day that is maintained for at least 1 hour.*

AND

After a period of stability or improvement on the ventilator, the patient has at least one of the following indicators of worsening oxygenation:

1) Increase in daily minimum* FiO2 of ≥ 0.20 (20 points) over the daily minimum FiO2 in the baseline period, sustained for ≥ 2 calendar days.

2) Increase in daily minimum* PEEP values of ≥ 3 cmH2O over the daily minimum PEEP in the baseline period†, sustained for ≥ 2 calendar days.

**Daily minimum defined by lowest value of FiO2 or PEEP during a calendar day that is maintained for at least 1 hour.*

†Daily minimum PEEP values of 0-5 cmH2O are considered equivalent for the purposes of VAE surveillance.

TIER 2: INFECTION-RELATED VENTILATOR-ASSOCIATED COMPLICATION (IVAC)

Patient meets criteria for VAC

A
N
D

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, the patient meets <u>both</u> of the following criteria:

1) Temperature > 38 °C or < 36°C, **OR** white blood cell count ≥ 12,000 cells/mm^3 or ≤ 4,000 cells/mm^3.

AND

2) A new antimicrobial agent(s)* is started, and is continued for ≥ 4 calendar days.

TIER 3A :POSSIBLE VENTILATOR-ASSOCIATED PNEUMONIA

Patient meets criteria for VAC and IVAC

AND

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections)
   - Defined as secretions from the lungs, bronchi, or trachea that contain ≥ 25 neutrophils and ≤ 10 squamous epithelial cells per low power field [lpf, x100].
   - If the laboratory reports semi-quantitative results, those results must be equivalent to the above quantitative thresholds.
   - See additional instructions for using the purulent respiratory secretions criterion in the VAE Protocol.

OR

2) Positive culture (qualitative, semi-quantitative or quantitative) of sputum*, endotracheal aspirate*, bronchoalveolar lavage*, lung tissue, or protected specimen brushing*

**Excludes the following:*

- Normal respiratory/oral flora, mixed respiratory/oral flora or equivalent
- *Candida* species or yeast not otherwise specified
- Coagulase-negative *Staphylococcus* species
- *Enterococcus* species

TIER 3B : PROBABLE VENTILATOR-ASSOCIATED PNEUMONIA

Patient meets criteria for VAC and IVAC

AND

On or after calendar day 3 of mechanical ventilation and within 2 calendar days before or after the onset of worsening oxygenation, ONE of the following criteria is met:

1) Purulent respiratory secretions (from one or more specimen collections —and defined as for possible VAP)

AND one of the following :

- Positive culture of endotracheal aspirate*, $\geq 10^5$ CFU/ml or equivalent semi-quantitative result
- Positive culture of bronchoalveolar lavage*, $\geq 10^4$ CFU/ml or equivalent semi-quantitative result
- Positive culture of lung tissue, $\geq 10^4$ CFU/g or equivalent semi-quantitative result
- Positive culture of protected specimen brush*, $\geq 10^3$ CFU/ml or equivalent semi-quantitative result

**Same organism exclusions as noted for Possible VAP.*

OR

2) One of the following (without requirement for purulent respiratory secretions):

- Positive pleural fluid culture (where specimen was obtained during thoracentesis or initial placement of chest tube and NOT from an indwelling chest tube)
- Positive lung histopathology
- Positive diagnostic test for *Legionella* spp.
- Positive diagnostic test on respiratory secretions for influenza virus, respiratory syncytial virus, adenovirus, parainfluenza virus, rhinovirus, human metapneumovirus, coronavirus

The aim of this new VAE definitions is to encourage survey in a single and concordant manner at all the adult hospitals as it changes the importance in mechanically ventilated adult patients from lung infection alone to a dependable, various set of conditions with a common thread – deterioration in respiratory function in mechanically ventilated.

We decided to start the surveillance with this new CDC algorithm for our study so that, we get an opportunity to learn more about its practical implications in VAP surveillance in our ICU.

THE ROLE OF SUBGLOTTIC SECRETION CLEARANCE IN PREVENTION OF VENTILATOR ASSOCIATED PNEUMONIA

VAP has become a common hindrance in intensive care unit and it is associated with prolonged ICU stay and hospital stay, increased mortality, the causative pathogens are multidrug-resistant and results in a huge increase in healthcare spending.

Focused VAP prevention measures that could reduce VAP incidence in critical care setting could positively affect patient safety in critical care units so, we should prioritize them.

As given in VAP bundle and other preventive recommendations, currently multiple interventions are in use to prevent VAP.

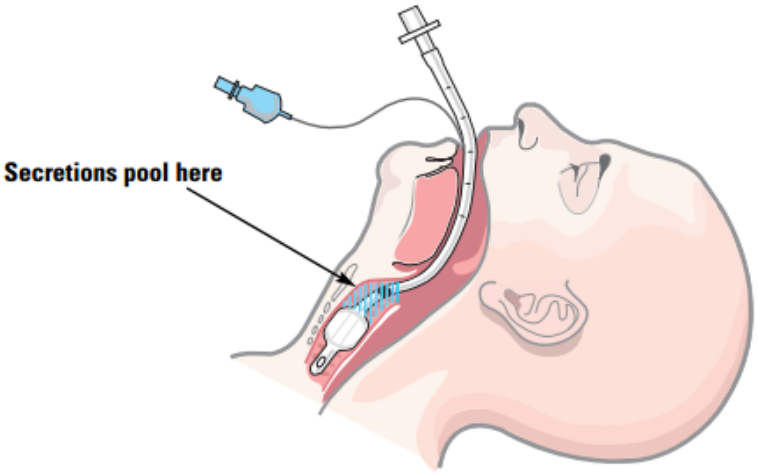
But, interferences affiliated to the endotracheal tube (ETT) itself, are attracting more interest, As one of the main risk factor for VAP development in ventilated patients is the endotracheal tube.

A standard endo-tracheal tube is reasoned to be a leading risk factor for VAP because,

- It acts as a storage tank for potentially infecting microorganisms,
- It acts a conduit between the oropharynx and the lower respiratory tract by bypassing inherent defenses,
- It modifies the ability to clear secretions as the patient cannot cough,
- By keeping the epi-glottis open, it allows oral-supraglottic secretions into the lower respiratory tract, and
- It does not prevent micro-aspiration of secretions and the eventual bio-film formation.

A standard or a conventional endo-tracheal tube ETT C:

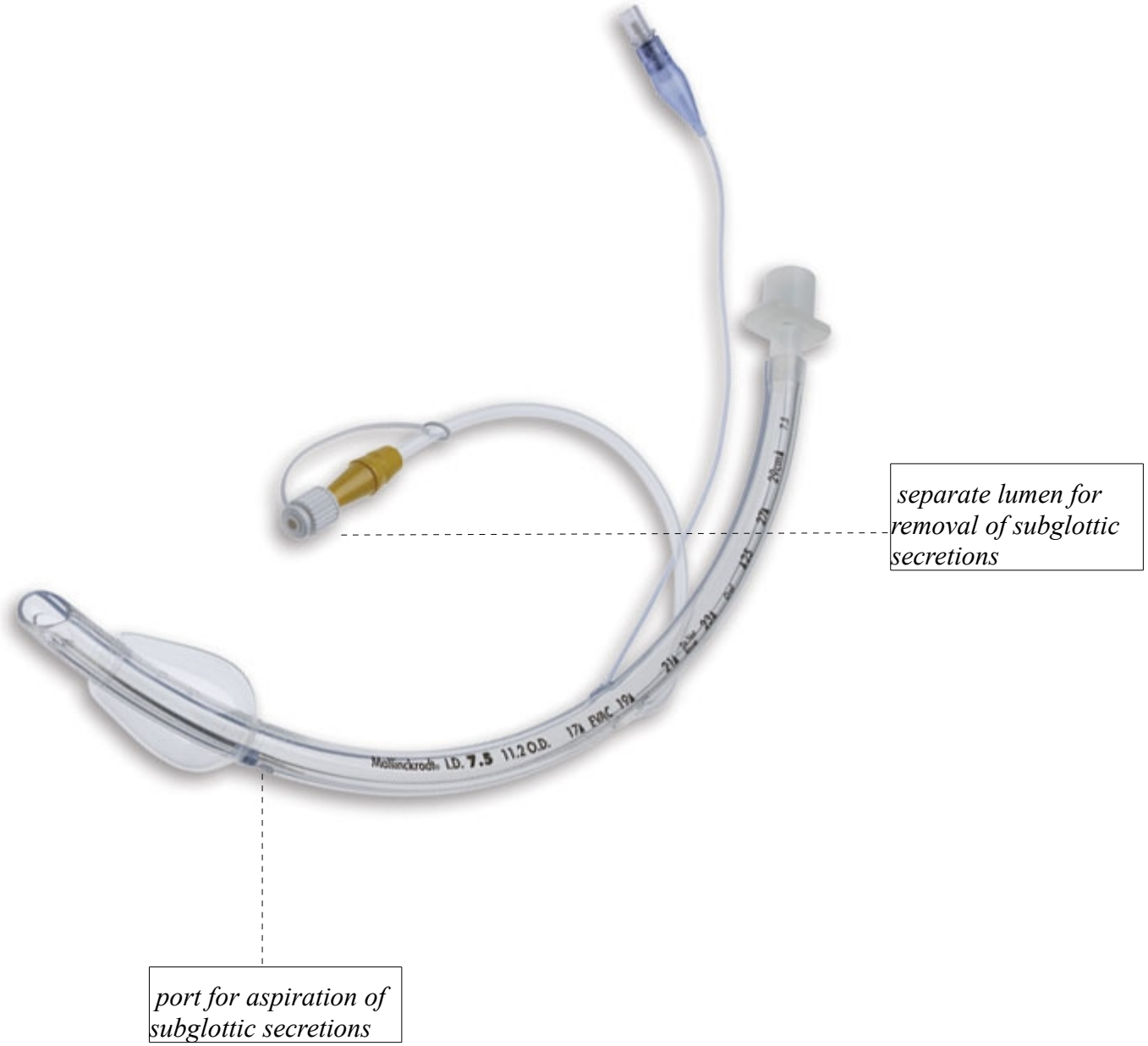
Figure showing- oropharyngeal secretion pooling above the cuff of the ETT C:



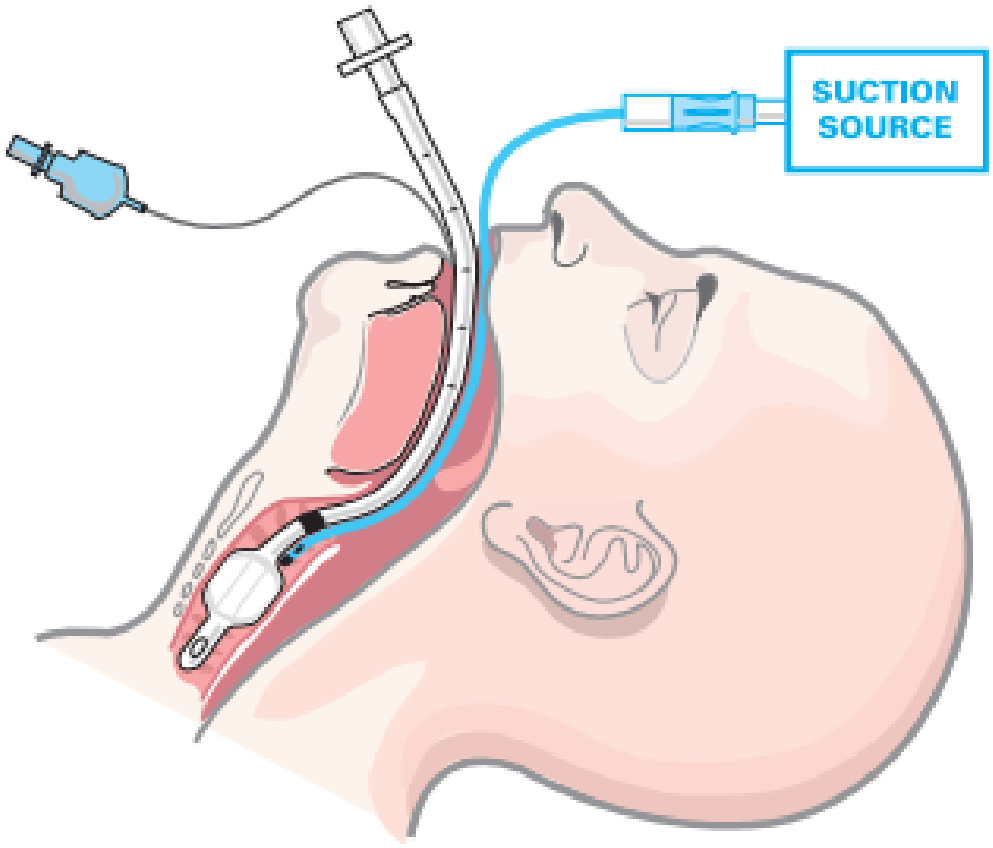
The subglottic secretion drainage or SSD is engineered to remove secretions accumulating above the ETT's cuff which is removed either by intermittent or continuous suctioning of in the subglottic area.

This intervention may cut down the risk of aspiration and prevent VAP.

Figure showing ETT SS-Subglottic Secretion Drainage:



These specially designed endo-tracheal tubes for subglottic secretion drainage possess an isolated dorsally placed lumen which opens above its cuff, through the port secretions can be aspirated by negative pressure as shown in the figure below.



Till date many studies had been done regarding subglottic secretion removal - in reducing incidence of ventilator associated pneumonia. Some of these studies showed decrease in the incidence of VAP (26–30)

While some other studies suggested when subglottic suction drainage is employed, a prolongation in the duration of time to the development of ventilator associated pneumonia is noted (26,31,32).

The benefit of subglottic secretion drainage in VAP prevention has been evidenced in 2 meta-analyses.

a) A study showing (33) showing a reduction of 50% in the risk of acquiring ventilator associated pneumonia-in this analysis 2,442 patients were evaluated from thirteen RCTs, but there was no reduction in mortality.

b) One more study (34) reported similar ventilator-acquired pneumonia reduction - were reported in a small meta analysis - mainly through reduction of ventilator associated pneumonia rates in the first 5 to 7 days after intubation.

Subglottic suction drainage seems to have its proven advantages and is currently recommend in the VAP bundle and it is reasonably cost-effective. It is not routinely used in high risk patients in whom the anticipated duration of ventilation is more than 48 hrs because lack of concrete evidence in its advantage, lack of availability and lack of consensus among healthcare providers of various specialties.

So, further research is required to learn more about the efficacy of using endo-tracheal with subglottic suction drainage in reducing the incidence of ventilator associated pneumonia. (35)

LABOROTARY DIAGNOSTIC MODALITIES

FOR VAP

The current VAP surveillance algorithm recommends three laboratory investigations with the notable omission of the chest x ray.

Chest x ray findings have been taken away in the recent CDC criteria because of its subjectivity without much increase in accuracy, In intensive care, chest radiography may sill play a clinical role, as the new CDC released VAP algorithm is intended for surveillance purposes only.

The recommended laboratory investigations are ,

WBC or white cell counts

- Leukocytosis

  WBC count above 12,000 /cu.mm (0r)

- Leukopenia

  -WBC count below 4,000/cu.mm.

Presence of purulent respiratory secretions

Secretion-sample obtained from the lungs, bronchus/bronchi and trachea when seen under low power field should contain more than 25 neutrophils and less than 10 squamous epithelial cells.

So, it is not merely the change in color and consistency of the respiratory secretions.

Quantitative microbial culture of

- Endo-tracheal secretion /aspirate,
- Pleural fluid specimen and
- Lung tissue sample.

Respiratory samples for microbial culture can be obtained using one or more of the following techniques(1)

1. ETA or Endotracheal aspirate is easiest to obtain where the specimen is sucked into a sterile container connected in line with the suction apparatus.
2. Broncho alveolar lavage (BAL): This technique requires bronchoscopic guidance for obtaining the sample.
3. Mini-broncho alveolar lavage (mini-BAL):Blindly performed since bronchoscopic guidance is not used.
4. Protected specimen brush (PSB): In this technique catheter with a brush at the tip is used to rub it against the bronchial wall.
5. Pleural fluid sample is obtained by a sterile aspiration technique and not from indwelling chest tubes or drains.
6. Lung biopsy even-though very rarely used for diagnosis of pneumonia is obtained by broncho-spic guidance or CT guided fine needle biopsy.

Threshold values recommended for probable ventilator associated pneumonia in quantitative culture reports are (6),

Technique used in sample collection	*Values needed for diagnosis*
Lung Tissue Sample:	10,000 cfu/gram of tissue
Bronchos-copy Specimens:	
B BAL- Broncho Alveolar Lavage	10,000 cfu/ml
B PBAL- Protected Broncho Alveolar Lavage	10,000 cfu/ml
B PSB- Protected Specimen Brushing	1,000 cfu/ml
Non Bronchos-copy (Blind) Specimens:	
Technique used in sample collection	*Values needed for diagnosis*
NB BAL-Broncho Alveolar Lavage	10,000 cfu/ml
BB PBAL- Protected Broncho Alveolar Lavage	10,000 cfu/ml
ETA – Endo-Tracheal Aspirate	100,000cfu/ml

cfu=colony forming units seen in the microbiology culture.

≥

ANTIMICROBIAL TREATMENT OF VENTILATOR-ASSOCIATED PNEUMONIA.

Although our research is limited to the surveillance of VAP, it is worthwhile to discuss the treatment and the difficulties associated with the antibiotic therapy (1)

The antibiotic therapy for VAP depends on few factors,

The duration of mechanical ventilation,

The local microbial pattern of the particular ICU and the hospital.

The sensitivity and resistant patterns of the above mentioned organisms and

More importantly in India the affordability of the patient for costlier broad spectrum antibiotic therapy.

The conventional understanding is to treat early-onset VAP with narrow spectrum antibiotics and late-onset VAP with broad spectrum antibiotics like carbepenams, vancomycin, teicoplanin, collistin etc.

But this practice is often not practical especially in referral centers and tertiary hospitals as a good number the patients receive antibiotics even before ICU admission.(1,7)

Also the fact that organisms like pseudomonas , acenetobacter, ESBL(*extended-spectrum-beta-lactamases)* producing gram-negative bacilli etc are inherently resistant to high end antibiotics or sometimes can develop resistance towards a particular antibiotic during therapy.

Apart from the cost factor the prolonged antibiotic therapy required to treat ventilator associated pneumonia can have its adverse effects like clostridium difficle colitis

fungal infection, renal toxicity, thrombocytopenia etc.

Although appropriate, individualized antibiotic therapy based on spectrum of coverage is needed for VAP, unnecessary broad-spectrum antibiotic usage should be avoided.

So, early de-escalation is strongly recommended as soon as the microbiology results are available or on clinical improvement, not only to recover costs but also to avoid development of resistance (7) .

Therefore, emphasis on continued research and sustained efforts on VAP prevention strategies cannot be over-emphasized in view the above discussed issues in antibiotic treatment of VAP.

MATERIALS AND METHODS

Detailed research plan:

STUDY DESIGN:

A Prospective Observational Study comparing the effect of endotracheal Tube with Subglottic Suction Port ETT SS vs standard Endotracheal tube ETT C on Incidence of Ventilator associated Pneumonia in patients ventilated for > 48 hrs in ICU.

SETTING:

Christian Medical College and Hospital, Vellore, Tami Nadu, India is a 2500 bedded hospital, with more than 100 beds in various intensive care units. It is a tertiary care center which caters to patients from all over India, South Asia, Middle East And some African countries.

This study is exclusively done on patients admitted to 13 bed Surgical ICU (SICU) & 6 bed AICU in Christian Medical College, Vellore. Recruited patients data will be collected and followed up till discharge from hospital.

Methods:

Adult patients admitted to intensive care unit (ICU) with duration of artificial respiration >48 hrs will be included in this study.

The type of ET tube (ETT C or ETT SS) used for intubation will be noted along with other variables like Patient details, diagnosis, per-existing illness, APACHE II score (score based on severity of illness and any other long standing illness), number of days on ventilator, number of days ICU stay & hospital stay.

Standard VAP bundle interventions to prevent ventilator associated pneumonia is given to all intubated patients in the ICU as a standard practice irrespective of type of endotracheal tube used for intubation ETT C or ETT SS.

Prior to our study, uniform objective surveillance algorithm for ventilator associated pneumonia did not exist in our ICU and Hospital.

Patients with fever, increased respiratory secretions, increased or decreased White cell count associated with sustained decrease in oxygenation will be screened for microorganisms from endo tracheal secretions.

Surveillance for Ventilator Associated Pneumonia in this study will be in accordance with the latest *"Surveillance for ventilator-associated events in the National Healthcare Safety Network (NHSN)"* guidelines released in Jan 2014.

Participants:

Inclusion criteria:

Adult Patients between 16 and 80 years of age who receive mechanical ventilation for > 48 hrs in ICU.

Exclusion criteria:

Patients intubated outside our hospital.

Patients suspected to have aspirated or at risk of aspiration prior to or during intubation.

Admitted with a diagnosis of community acquired pneumonia.

Pregnant women & Children.

Patients recruited to other studies.

Refusal of assent.

Primary outcome:

Incidence of VAP or Ventilator Associated Pneumonia and

Secondary outcomes:

All VAEs - Ventilator Associated Events

VAC-Ventilator Associated Condition ,

IVAC- Infection related Ventilator Associated Condition ,

Possible VAP- Ventilator Associated Pneumonia and

Probable VAP- Ventilator Associated Pneumonia

and

Duration of mechanical ventilation,

Length of ICU stay,

Length of hospital stay and

In hospital mortality.

Sample size:

To test whether any significance difference in the incidence of VAP among the two groups, the minimum required samples to be studied is 80 in each group. So the total sample size was determined as 160.

The formula used for the sample size calculation was

$$n = \frac{\left\{ Z_{1-\frac{\alpha}{2}} \sqrt{2\,\bar{P}\,(1-\bar{P})} + Z_{1-\beta} \sqrt{P_1\,(1-P_1) + P_2\,(1-P_2)} \right\}^2}{(P_1 - P_2)^2}$$

Where,

$$\bar{P} = \frac{P_1 + P_2}{2}$$

P_1 : Proportion in the first group

P_2 : Proportion in the second group

α : Significance level

$1-\beta$: Power

Here p1 = 0.30, p2=.516, type 1 error =5% and power=80%.

(Reference: Zheng et al 2008 (8))

Statistical methods:

The overall incidence of VAE and VAP per 1000 ventilator days was calculated using the formula given by CDCs NSHN in the new VAP surveillance algorithm.

VAE =no of events/ no of ventilator days x 1000 ventilator days

The incidence of VAP in two groups was compared using two sample proportion test.

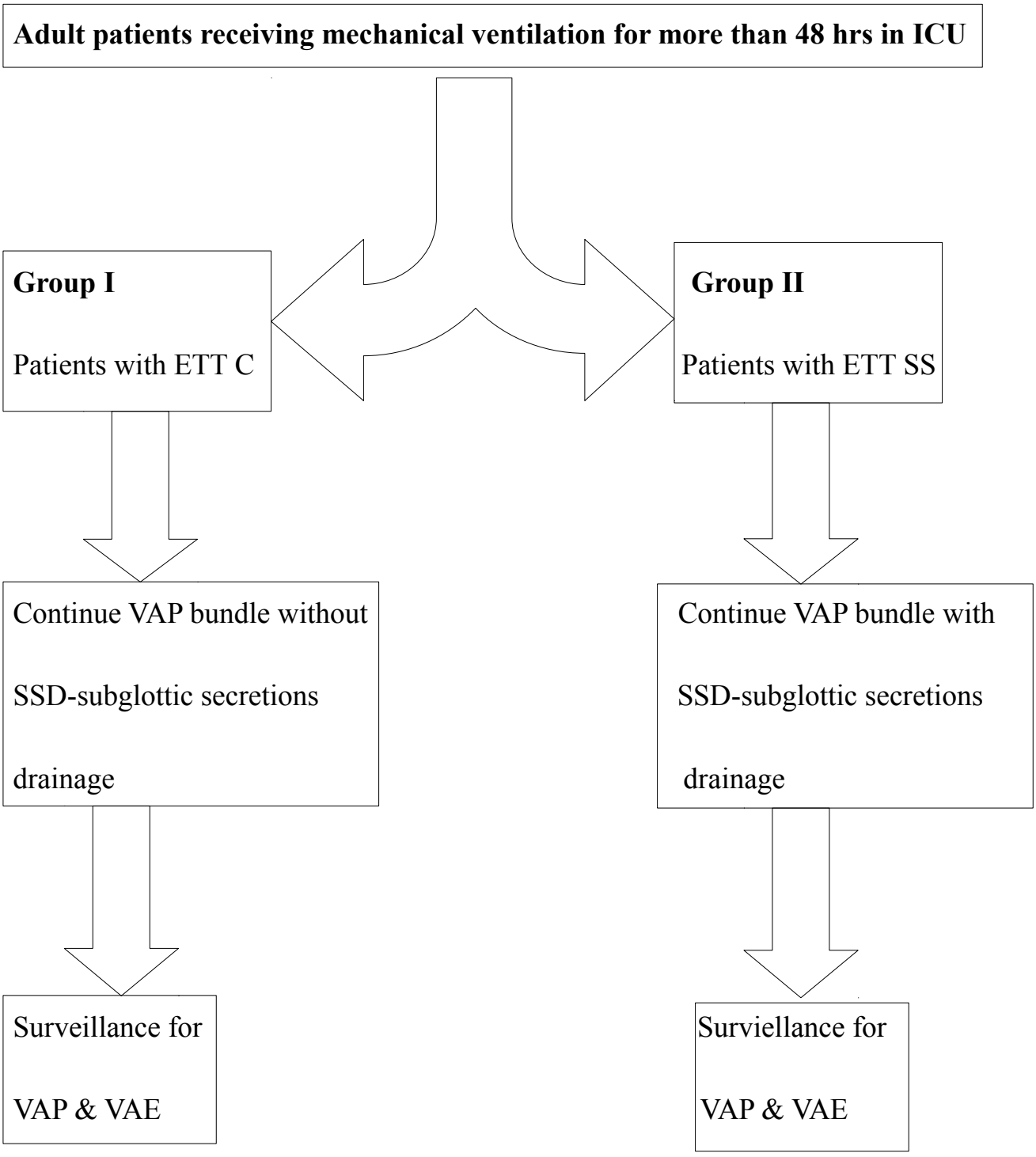
The association between the clinical variables and the incidence of VAP was analyzed using Chi-square test.

Logistic regression analysis was used to calculate the relative risk and 95% CI of VAP incidence.

Descriptive statistics and frequencies was used to represent all the variables along with appropriate diagrams.

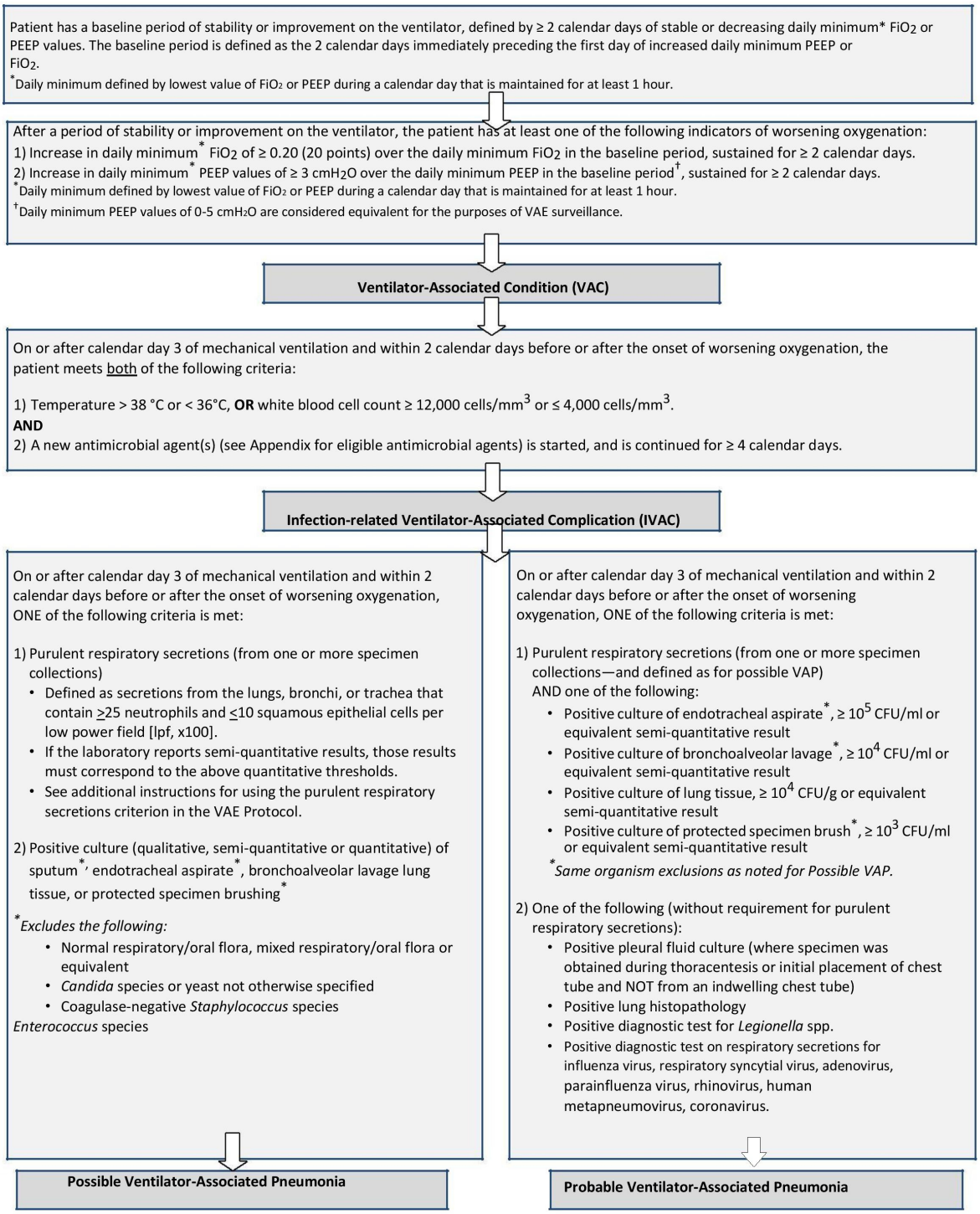
SPSS 17.0 software is used for data analysis.

Detailed diagrammatic algorithm of the study design:



The following CDC algorithm is used to find out the incidence of VAP and VAEs in our ICU for this study:

Ventilator-Associated Events (VAE) Surveillance Algorithm:



RESULTS

Between April 2014 to September 2014 one hundred patients required mechanical ventilation (43 in ETT SS group and 57 in ETT C group) for more than 48 hours were recruited into our study.12 patients were later excluded from the study (all ETT C)as they were re-intubated with ETT SS after 24 hours due to various reasons like

- Tube Block,
- Failed extubation,
- Accidental extubation,
- Cuff damage,
- Tracheotomy etc.

Data of 88 patients were analysed of which, 43 of them in ETT SS group and 45 others in ETT C group.

DEMOGRAPHIC VARIABLES AMONG STUDY PARTICIPANTS:

GENDER:

Among the patients recruited in the ETT SS group there were 10 females and 33

males and in ETT C there were 14 females and 31 males, with the 'p' value = 0.0408. There was significant gender difference within the two groups, depicted in the following table.1

TABLE.1: GENDER

E.T.TUBE TYPE	ETT SS	ETT C	TOTAL
MALE	10 (23.3%)	14 (27.3%)	24 (27.3 %)
FEMALE	33 (76.8%)	31 (68.9%)	64 (72.8%)
TOTAL	43 (100%)	45 (100%)	88 (100 %)

AGE:

The mean age of patients in ETT SS group was 41.4 ± 14.72 years compared to ETT C group 48.02 ± 15.92 years.

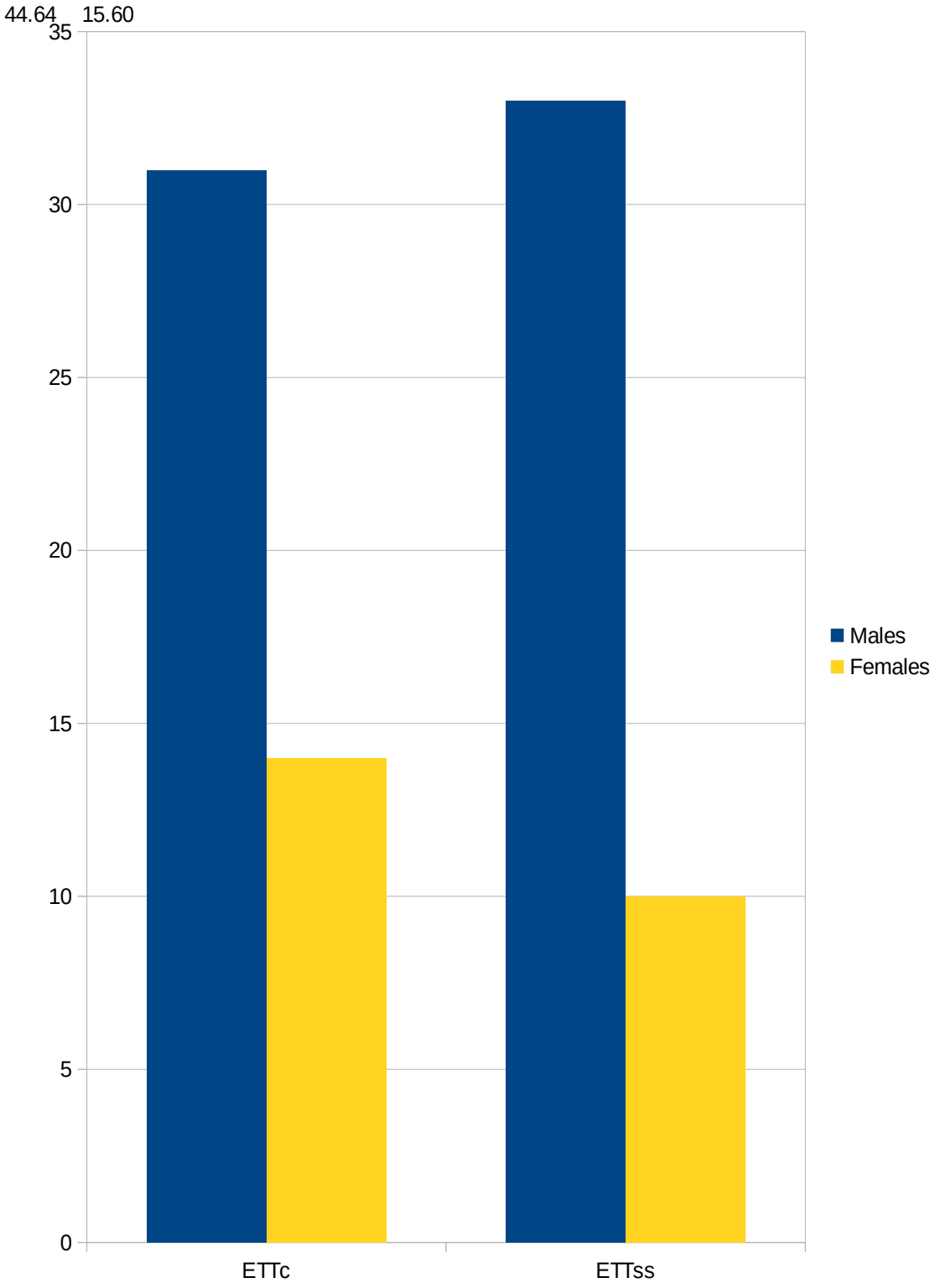
ETT SS group patients were significantly older than ETT C group.

Depicted in table.2.

TABLE.2: AGE

ETT TYPE	ETT C	ETT SS	p-value
AGE in years	**41.4 ± 14.72**	**48.02 ± 15.92**	**0.0458**

Figure showing mean age distribution between two patient groups ETT C and ETT SS



PREVALENCE OF ETA-MICROORGANISMS IN THE STUDY POPULATION:

A quantitative culture of more than 1,00,000 colony-forming units from a endotracheal aspirate is considered significant. In the study group, the distribution of patients with significant quantitative cultures is shown in the table below. All respiratory secretion specimens were ETA- endo tracheal aspirates collected by protected telescoping catheter sampling. The number of positive cultures and the organisms grown are given the following table.3.

TABLE.3:PREVALENCE OF MICROORGANISMS :

ETT TYPE	ETT SS	Number of Positive cultures	ETT C	Number of Positive cultures
Micro-organisms	Acenetobacter Baumanii	5	Acenetobacter Baumanii	5
	NFGNB or Non Fermenting Gramnegative Bacilli	4	NFGNB or Non Fermenting Gramnegative Bacilli	1
	Pseudomonas species	2	Pseudomonas species	0
	Klebsiella	1	Klebsiella	1
	E.coli	0	E.coli	2
TOTAL		12		9

CLINICAL STATUS OF PARTICIPANTS

There were few significant differences in the baseline characteristics between ETT C and ETT SS patients.

As for as the associated co-morbid illnesses were concerned there were differences between the two groups showing statistical significance .

The ETT C group had lesser number of patients with HTN -Hyper tension 5 0ut of 45 (11 %) compared to ETT SS group 13 out of 43 (30.23 %) 'p' value = 0.026 which was statistically significant, shown in the following table.4.

TABLE.4:

ETT TYPE	**ETT SS**	**ETT C**	**p-value**
HYPERTENSION	**13 (30.23%)**	**5 (11.11%)**	**0.026**

The ETT C group had lesser number of patients with DM- diabetes mellitus 8 out of 45 (17.78%) compared to ETT SS group 15 out of 43 (34.88 %) 'p' value = 0.067 which turned out to be not statistically significant as shown in table.5:

TABLE.5:

ETT TYPE	ETT SS	ETT C	P-value
DM	15 (34.88%)	8 (17.78%)	0.067

Among other co-morbid conditions there were significant differences between the two groups in the number of patients with Tuberculosis-TB,Chronic Liver Disease-CLD and Thyroid disease as they were significantly higher in ETT SS group compared to ETT C group.

Co-morbid illnesses in the two groups are shown in the table.6:

TABLE.6: COMORBID ILLNESS:

TYPE OF ETT	ETT SS	ETT C	p-values
IHD	5 (11.6%)	4 (8.9%)	0.67
CLD	2 (4.65%)	0	0.143
CKD	3 (6.98%)	4 (8.89%)	0.74
COPD	1 (2.23%)	2 (4.44%)	0.582
TB	4 (9.3%)	0	0.037
THYROID DISEASE	0	2 (2.44%)	0.162
ATRIAL FIBRILATION	3 (6.98%)	0	0.071

The APACHE II SCORE-"Acute Physiology and Chronic Health Evaluation II" Score was used to measure the severity of disease in patients admitted to our ICU. The mean Apache II score did not show any statistical significance between the two groups even though it was higher in ETT SS group, as given in the table.7: below.

TABLE.7:

ETT TYPE	ETT C	ETT SS	p-value
APACHE II score	**21.84 ± 8.49**	**26.14 ± 10.97**	**0.0520**

PRIMARY OUTCOME

PRIMARY OUTCOME:

INCIDENCE OF VAP:

In spite of a positive microbial growth on 21 occasions in recruited patients (both the groups together), with cfu > 100,000 in ETA, after 48 hours of ventilation as shown in table.3 earlier, when on applying CDC VAP Surveillance algorithm only 2 out of 88 patients had probable VAP, and only 8 patients in total had VAE- Ventilator Associated Events.

So, in our ICU for a period of six months between April l2014 to September 2014, **the incidence of VAP was 4.24 per 1000 ventilator days**.

Two events of Probable -VAP ventilator associated pneumonia were present in ETT C group and none in ETT SS group.

Therefore, **the incidence of VAP in ETT C group was higher 4.44% compared to ETT SS group which was 0%** because of the small incidence in both groups p value could not be calculated, shown in Table.8.

TABLE.8: THE INCIDENCE OF VAP IN BOTH GROUPS

VENTILATOR ASSOCIATED PNEUMONIA	TYPE OF ENDOTRACHEAL TUBE USED		TOTAL
PROBABLE- **VAP**	**0**	**2** **(4,44%)**	**2** **(2.3%)**

SECONDARY OUTCOMES

SECONDARY OUTCOMES:

INCIDENCE OF VAE:

The overall incidence of **VAE (**VAC+IVAC+POSSIBLE VAP+PROBABLE VAP**) was 16.94 per 1000 ventilator days**.

The above mentioned incidence was calculated using the formula given by CDC's National Healthcare Safety Network -NSHN for surveillance of ventilator associated events- VAE.

$$\text{INCIDENCE OF VAE} = \frac{\text{TOTAL NO EVENTS} \quad X \quad 1000 \text{ VENTILATOR DAYS}}{\text{TOTAL NO VENTILATOR DAYS}}$$

The VAEs summary,

- Four events of Ventilator associated condition (VAC) were present in ETT SS group and none in ETT C group.
- One event of Infection related ventilator associated condition (IVAC) was present in both groups.
- Possible -VAP ventilator associated pneumonia was not present in either group.
- Two events of Probable -VAP ventilator associated pneumonia were present in ETT C group and none in ETT SS group. Shown in the following table.9.

TABLE.9:

VAE INCIDENCE AMONG TWO GROUPS:

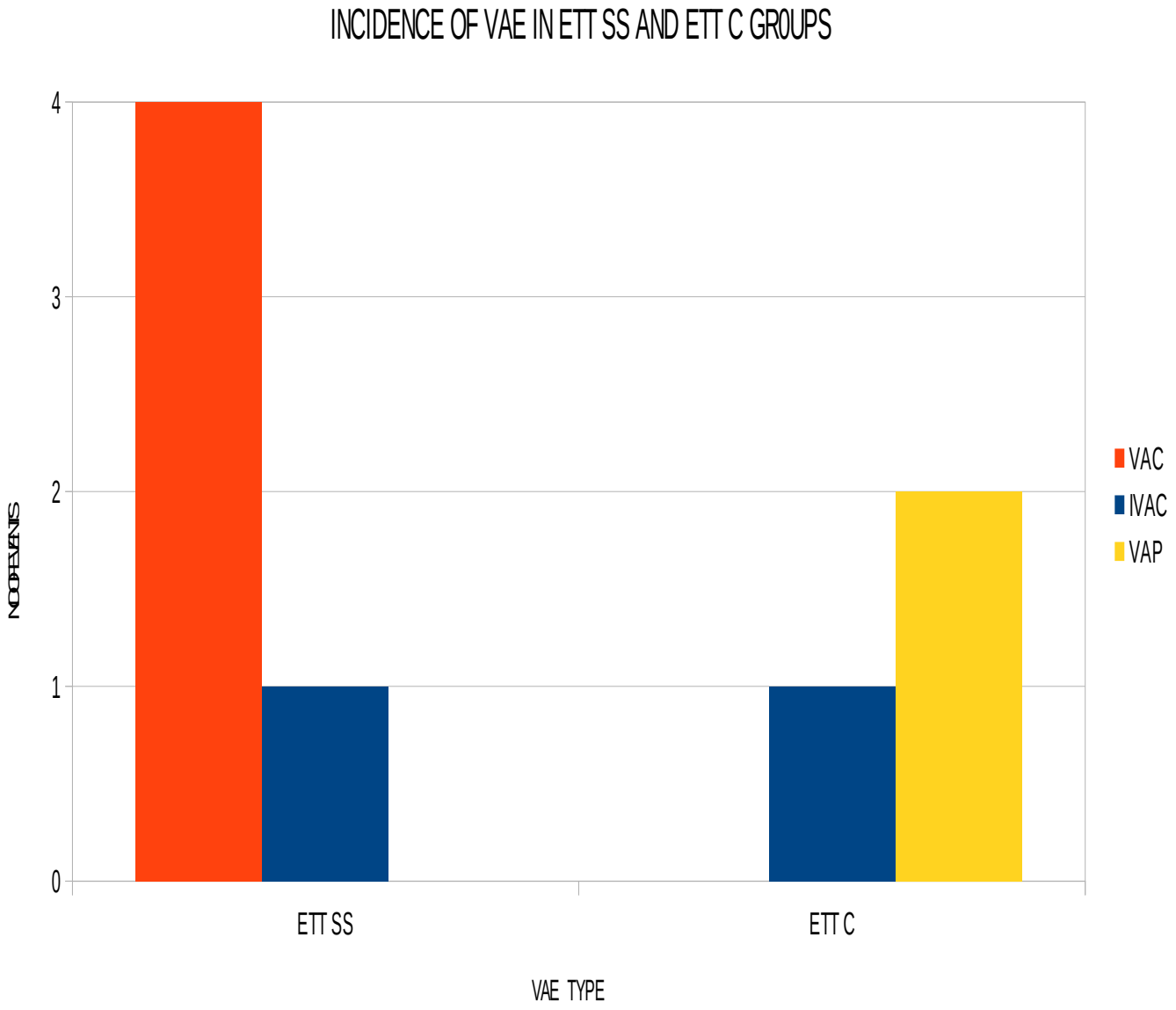
VENTILATOR ASSOCIATED EVENTS-VAE	TYPE OF ENDOTRACHEAL TUBE USED		TOTAL
	ETT SS	**ETT C**	
VAC	4 (9.30%)	0	4 (4.55%)
IVAC	1 (2.32%)	1 (2.22%)	2 (2.27%)
POSSIBLE- VAP	0	0	0
PROBABLE- VAP	0	2 (4,44%)	2 (2.3%)
NO VAE	38 (88.37%)	42 (93.33%)	80 (90.85%)

There were 5 Ventilator associated events – VAE in ETT SS group out of 42 patients vs 3 Ventilator associated events – VAE in ETT C out of 45 patients which was not statistically significant with p-value of 0.41794, shown in table.10.

TABLE.10: NUMBER OF VENTILATOR ASSOCIATED EVENTS IN EACH GROUP

	TYPE OF TUBE USED		**p-value**
	ETT SS	**ETT C**	
VAE	**5/43 = 11.6 %**	**3/45 = 6.6 %**	**0.41794 (proportion test was used)**

Figure below shows the incidence of VAE among ETT SS & ETT C groups:



DURATION OF MECHANICAL VENTILATION:

The ETT SS group had statistically significant longer duration of mechanical ventilation 6.91 ± 5.68 days, compared to the ETT C group patients 3.89 ± 2.01 days, given in the table.11 below

TABLE.11: DURATION OF MECHANICAL VENTILATION

Type of the tube used	**ETT C**	**ETT SS**	**p-value**
MV Days	**3.89 ± 2.01**	**6.91 ± 5.68**	**0.0009**

LENGTH OF ICU STAY;

The mean length of ICU stay was statistically significant as, ETT SS group patients had longer length of ICU stay 7.53 ± 6.29 days, compared to ETT C group patients 4.60 ± 2.28 days, with p-value of 0.006 given in table.12

TABLE.12: LENGTH OF ICU STAY

Type of the tube used	**ETT C**	**ETT SS**	**p-value**
ICU Stay	**4.60 ± 2.28**	**7.53 ± 6.29**	**0.0061**

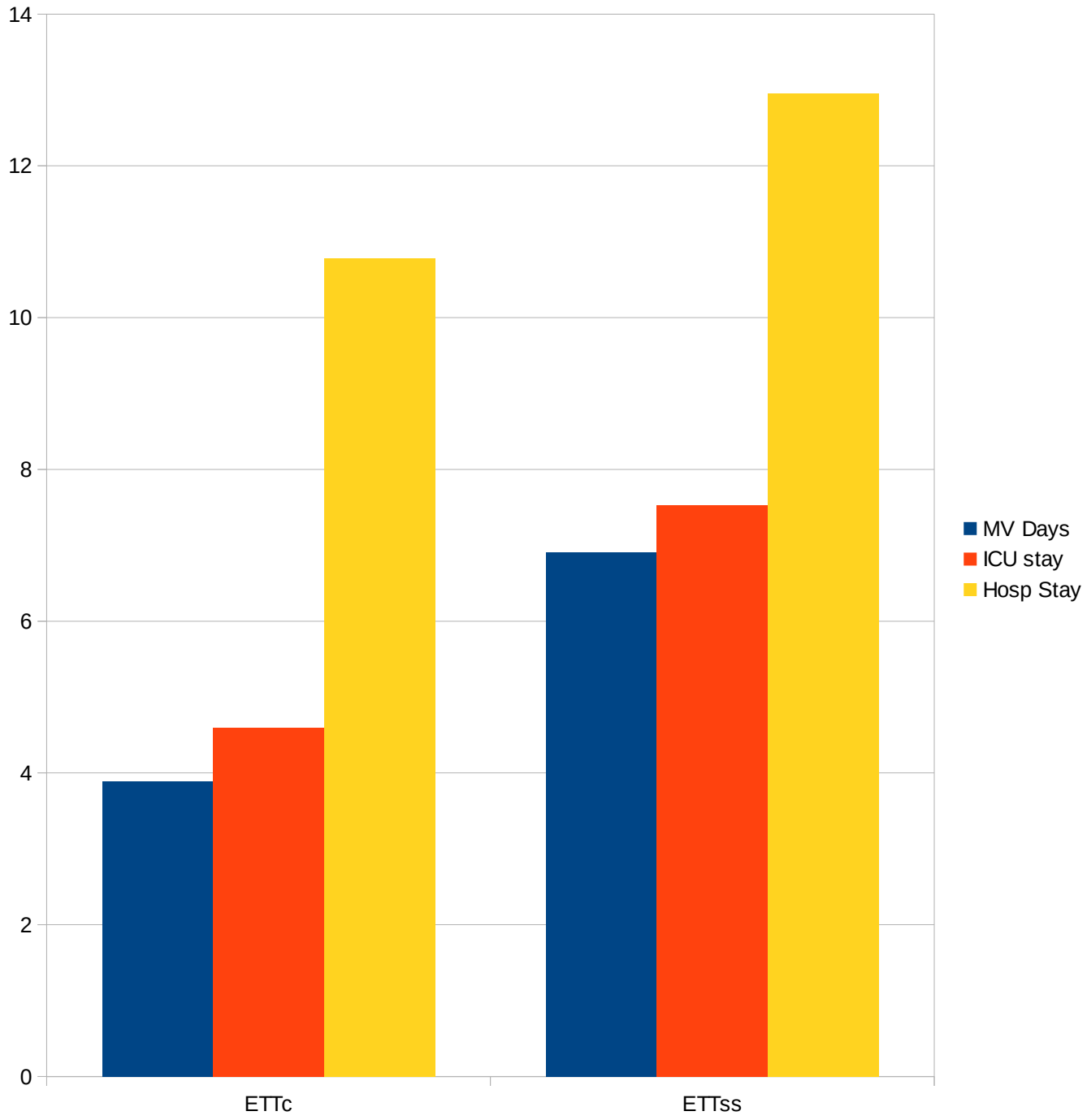
LENGTH OFHOSPITAL STAY:

But, the mean length of hospital stay was comparable between two groups, ETT C 10.78 ± 6.60 days vs ETT SS 12.95 ± 8.15 days, showing no statistically significant difference, as seen in the table.13 below.

TABLE.13: LENGTH OFHOSPITAL STAY

Typ e of the tube used	**ETT C**	**ETT SS**	**p-value**
Hospital Stay	**10.78 ± 6.60**	**12.95 ± 8.15**	**0.127**

Figure representing the duration of mechanical ventilation, ICU stay and hospital stay among ETT SS and ETT C:



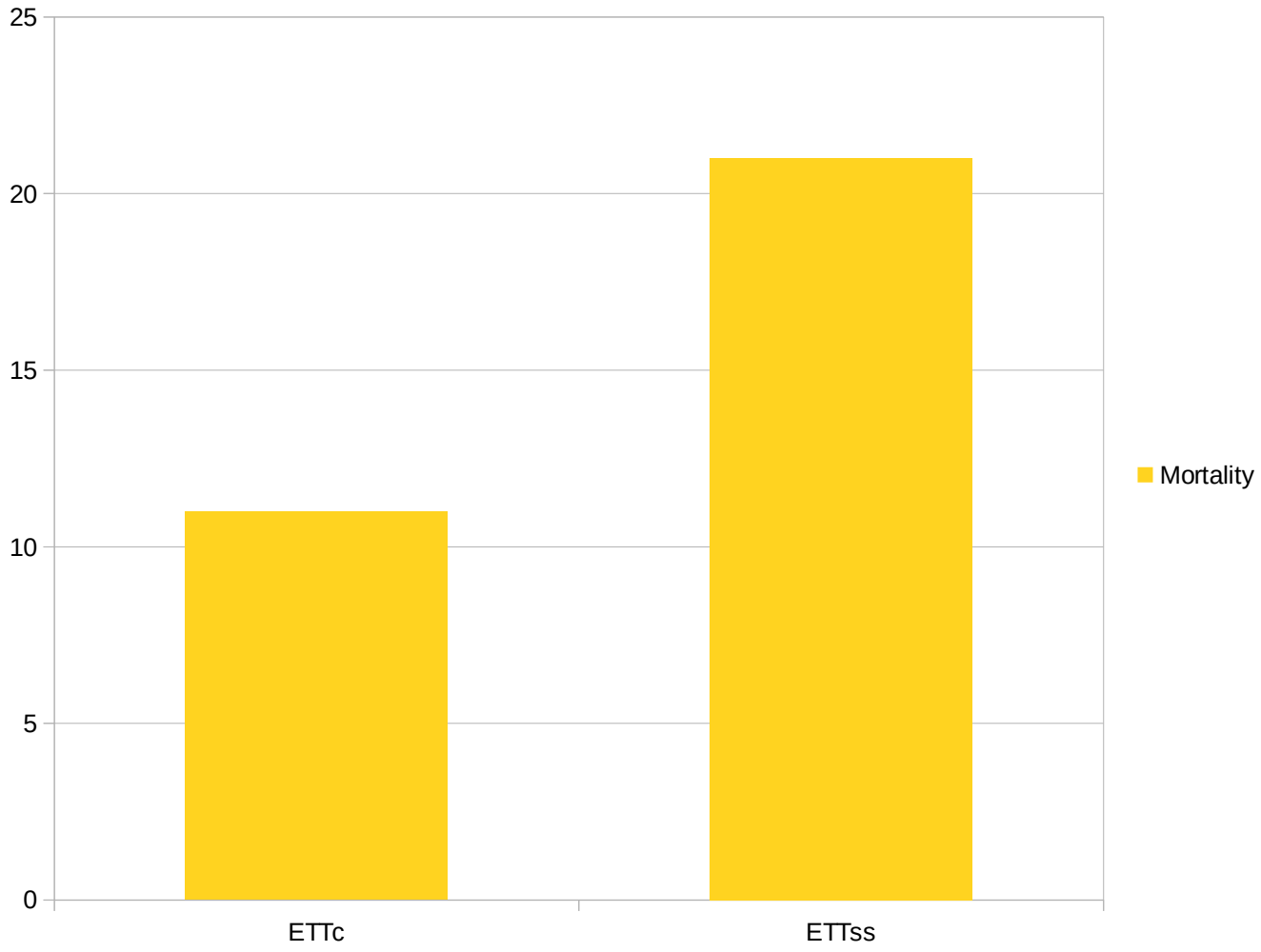
IN HOSPITAL MORTALITY:

While 21 patients died in the hospital in the ETT SS group, only 11 patients died in the hospital in the ETT C group, with p-value of 0.017, as shown in table.14 below.

TABLE.14: IN HOSPITAL MORTALITY

Type of the tube used	**ETT C**	**ETT SS**	**p-value**
Mortality	**11**	**21**	**0.017**

Figure showing in hospital mortality among two groups of patients:



DISCUSSION

Prevention of VAP needs a multipronged approach and we set out to see if the use of ETT SS as part of VAP bundle is associated with lesser incidence of VAP. With the change in the surveillance definition from the CDC, the future reporting will be based on the new definition and we have studied with the new definition.

With data already available in favor of ETT SS, we set out to see if this finding is applicable to our Indian set up.

We could not recruit the required number of patients due to time limit for submission of thesis. The interim analysis is underpowered, but is showing a trend favoring use of ETT SS. The study is ongoing and definite recommendations will be made on recruitment of the necessary number of patients.

In our observational study the use of endo-tracheal tube subglottic drainage ETT SS was associated with reduced incidence of VAP in comparison with the standard endo-tracheal tube ETT C.

The patients in ETT SS were older, had a higher sickness score, had more co-morbid illnesses and were ventilated for a longer period. In spite of this they had lesser incidence of VAP. The mortality among this group was higher but this clearly is not related to pneumonia. The higher mortality may be related to the comorbidities and the higher sickness score.

But, being an underpowered observational study, with inadequate sample size to

show statistically significant results, as results are obtained by interim analysis we decided to continue surveillance in our ICU and reserve the recommendation of its mandatory use in other ICUs, Operation Theaters, Emergency Department e.t.c, till the required sample size is achieved and results are re-analyzed.

The incidence of VAP in our ICU was 4.24 per 1000 ventilator days which is comparable to the incidence reported in National Healthcare Safety Network facilities in U.S.A (7).

This showed that in our ICU the VAP prevention strategies such as VAP BUNDLE interventions are implemented effectively.

The incidence of VAP is lesser than expected in our ICU (8,9)., the VAP incidence calculated in all the ICUs put together in our hospital was about 40% the previous year (quoted earlier-This cannot be compared) showing an improvement HAI awareness among the health-care personnel in our ICU and overall implementation and compliance to HAI prevention practices.

The overall incidence of ventilator associated events was not significantly different the two groups as evident in the interim analysis but, as the surveillance for VAE is being continued, it is only appropriate to wait till its completion and re-analyse the results prior to making a strong hypothesis.

As mentioned earlier in the previous section even-though the two study groups

were not comparable the in terms of demographics and clinical statuses. The ETT SS group patients were significantly older and sicker compared to ETT C group on ICU admission.

As significantly larger number patients in ETT SS group had co-morbid illnesses such as Hypertension, Ischemic Heart Disease, Chronic Liver Disease, Tuberculosis etc and they also had higher mean APACHE II scores compared to ETT C group, not all these factors were of statistical importance but, might be of clinical importance(35) .

Moreover, the increased length of mechanical ventilation and longer ICU stay in t ETT SS group compared to ETT C can be explained by the fact that, more number of older and sicker patients were in that group.

So, longer time spent on ventilator, increased length of ICU stay associated with sicker and older patients of ETT SS group could have resulted in significantly higher hospital mortality in this group.

It is encouraging to see that there is a trend towards lesser VAP with the use of ETT SS. This if confirmed after recruiting the necessary number of patients will be recommended to other areas of Hospitals for patients who will need mechanical ventilation in the ICU.

Being an under-powered study no strong recommendation is made for the

regular use of ETT SS or subglottic secretion removal for VAP prevention at this point of time.

LIMITATIONS

- The results of our study was obtained by interim analysis of data for the sake completion of post graduate dissertation.
- Being an under powered study no strong recommendation is made for the regular use of ETT SS or subglottic secretion removal for VAP prevention.
- This is an observational study limited to one ICU. A further study involving more centers will be more meaningful.
- The use of the new CDC VAP algorithm in immune-suppressed or patients with hematological disease with WBC counts in the extremes of spectrum is yet to be determined.

CONCLUSION

- We conclude at the end of our study that, the incidence of VAP- ventilator associated pneumonia showed a reduced trend with the use of ETT SS- Endo-tracheal tube with subglottic suction drainage in comparison with standard endo-tracheal tube ETT C.
- The overall incidence of ventilator associated events was not significantly different the two groups as evident in the interim analysis
- our study showed that in our ICU the vap prevention strategies such as Vap Bundle interventions are implemented effectively
- Strong recommendations regarding the use of ETT SS could not be made since, the sample size required for statistical significance was not achieved.
- The surveillance of VAP with the use of recent CDC algorithm will continue for the surveillance of VAP in our ICU till the required sample size is achieved.

REFERENCES

1. Prevention of hospital-acquired infectionsWHO [Internet]. [cited 2014 Sep 12]. Available from: http://www.who.int/csr/resources/publications/whocdscsreph200212.pdf

2. Rosenthal VD, Maki DG, Salomao R, Moreno CA, Mehta Y, Higuera F, et al. Device-Associated Nosocomial Infections in 55 Intensive Care Units of 8 Developing Countries. Ann Intern Med. 2006 Oct 17;145(8):582–91.

3. Mani R, Saxena P. Preventing hospital acquired infections: A challenge we must accept. Indian J Crit Care Med. 2014;18(3):125.

4. Saloojee H, Steenhoff A. The health professional's role in preventing nosocomial infections. Postgrad Med J. 2001 Jan 1;77(903):16–9.

5. National Guideline Clearinghouse | Prevention of ventilator-associated pneumonia. Health care protocol. [Internet]. [cited 2014 May 3]. Available from: http://www.guideline.gov/content.aspx?id=36063

6. Strategy for the Control of Antimicrobial Resistance in Ireland, Health Protection Surveillance Centre (Ireland). Guidelines for the prevention of ventilator-associated pneumonia in adults in Ireland. Dublin: Health Protection Surveillance Centre; 2011.

7. CDC - ACH Surveillance for VAP Event - NHSN [Internet]. [cited 2014 Aug 22]. Available from: http://www.cdc.gov/nhsn/acute-care-hospital/vap/

8. Kalanuria AA, Zai W, Mirski M. Ventilator-associated pneumonia in the ICU. Crit Care. 2014;18(2):208.

9. Ventilator Associated Pneumonia – an Overview | British Journal of Medical Practitioners [Internet]. [cited 2014 Sep 14]. Available from: http://www.bjmp.org/content/ventilator-associated-pneumonia-overview

10. Bouza E, Brun-Buisson C, Chastre J, Ewig S, Fagon JY, Marquette CH, et al. Ventilator-associated pneumonia European Task Force on ventilator-associated pneumonia Chairmen of the Task Force: A. Torres and J. Carlet. Eur Respir J. 2001;17(5):1034–45.

11. Melsen WG, Rovers MM, Groenwold RH, Bergmans DC, Camus C, Bauer TT, et al. Attributable mortality of ventilator-associated pneumonia: a meta-analysis of individual patient data from randomised prevention studies. Lancet Infect Dis. 2013 Aug;13(8):665–71.

12. Bansode BR. Ventilator-Associated Pneumonia (VAP). [cited 2014 Sep 18]; Available from: http://apiindia.org/pdf/medicine_update_2011/72_ventilator_associated_pneumonia.pdf

13. Mietto C, Pinciroli R, Patel N, Berra L. Ventilator associated pneumonia: evolving definitions and preventive strategies. Respir Care. 2013;58(6):990–1007.

14. Gil-Perotin S, Ramirez P, Marti V, Sahuquillo JM, Gonzalez E, Calleja I, et al. Implications of endotracheal tube biofilm in ventilator-associated pneumonia response: a state of concept. Crit Care. 2012;16(3):R93.

15. Kallet RH, Quinn TE. The gastrointestinal tract and ventilator-associated pneumonia. Respir Care. 2005;50(7):910–23.

16. Critical Analysis of the Factors Associated with Enteral Feeding in Preventing VAP: A Systematic Review [Internet]. [cited 2014 Sep 20]. Available from: http://homepage.vghtpe.gov.tw/~jcma/72/4/171.pdf

17. Khalid I, Doshi P, DiGiovine B. Early Enteral Nutrition and Outcomes of Critically Ill Patients Treated With Vasopressors and Mechanical Ventilation. Am J Crit Care. 2010 May 1;19(3):261–8.

18. Unnewehr H, Rittirsch D, Sarma JV, Zetoune F, Flierl MA, Perl M, et al. Changes and Regulation of the C5a Receptor on Neutrophils during Septic Shock in Humans. J Immunol. 2013 Mar 11;1200534.

19. Morris AC, Brittan M, Wilkinson TS, McAuley DF, Antonelli J, McCulloch C, et al. C5a-mediated neutrophil dysfunction is RhoA-dependent and predicts infection in critically ill patients. Blood. 2011;117:5178–88.

20. American Thoracic Society IDS of A. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. Am J Respir Crit Care Med. 2005;171:388–416.

21. Ahrens T, Kollef M, Stewart J, Shannon W. Effect Of Kinetic Therapy on Pulmonary Complications. Am J Crit Care. 2004 Sep 1;13(5):376–82.

22. Perry D, Borchet K, Patel B, Burke S, Chick K, others. Pressure Ulcer Prevention and Treatment Protocol [Internet]. EUA. Institute For Clinical Systems Improvement (ICSI); 2012 [cited 2014 Oct 3]. Available from: https://www.icsi.org/_asset/6t7kxy/PresUlcerTrmt-Interactive0112.pdf

23. Ventilator-Associated Pneumonia Radiologic Diagnosis-Wunderink_2000.pdf [Internet]. [cited 2014 Sep 21]. Available from: http://www0.sun.ac.za/Physiotherapy_ICU_algorithm/Documentation/Changes%20on%20CxR/VAP/References/Wunderink_2000.pdf

24. Fàbregas N, Ewig S, Torres A, El-Ebiary M, Ramirez J, de la Bellacasa JP, et al. Clinical diagnosis of ventilator associated pneumonia revisited: comparative validation using immediate post-mortem lung biopsies. Thorax. 1999;54(10):867–73.

25. Berton DC, Kalil AC, Cavalcanti M, Teixeira PJ. Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia Chocrane Database Syst Rev CD006482. 2012;

26. Kirtland SH, Corley DE, Winterbauer RH, Springmeyer SC, Casey KR, Hampson NB, et al. The diagnosis of ventilator-associated pneumonia : A comparison of histologic, microbiologic, and clinical criteria. Chest. 1997 Aug 1;112(2):445–57.

27. A'Court C, Garrard CS. Nosocomial pneumonia in the intensive care unit: mechanisms and significance. Thorax. 1992 Jun;47(6):465–73.

28. CDC - ACH Surveillance for VAP Event - NHSN [Internet]. [cited 2014 Aug 22]. Available from: http://www.cdc.gov/nhsn/acute-care-hospital/vap/

29. Ventilator-associated Pneumonia (VAP) Events - 10-VAE_FINAL.pdf [Internet]. [cited 2014 Aug 22]. Available from: http://www.cdc.gov/nhsn/pdfs/pscManual/10-VAE_FINAL.pdf

30. Bo H, He L, Qu J. [Influence of the subglottic secretion drainage on the morbidity of ventilator associated pneumonia in mechanically ventilated patients]. Zhonghua Jie He He Hu Xi Za Zhi Zhonghua Jiehe He Huxi Zazhi Chin J Tuberc Respir Dis. 2000 Aug;23(8):472–4.

31. Juneja D, Javeri Y, Singh O, Nasa P, Pandey R, Uniyal B. Comparing influence of intermittent subglottic secretions drainage with/without closed suction systems on the incidence of ventilator associated pneumonia. Indian J Crit Care Med Peer-Rev Off Publ Indian Soc Crit Care Med. 2011;15(3):168–72.

32. Lorente L, Lecuona M, Jiménez A, Mora ML, Sierra A. Influence of an Endotracheal Tube with Polyurethane Cuff and Subglottic Secretion Drainage on Pneumonia. Am J Respir Crit Care Med. 2007 Dec;176(11):1079–83.

33. Yang C, Qiu H, Zhu Y, Huang Y, Xu X, Gao L. [Effect of continuous aspiration of subglottic secretions on the prevention of ventilator-associated pneumonia in mechanically ventilated patients: a prospective, randomized, controlled clinical trial]. Zhonghua Nei Ke Za Zhi. 2008 Aug;47(8):625–9.

34. Zheng R-Q, Lin H, Shao J, Chen Q-H, Lu N-F, Yu J-Q. [A clinical study of subglottic secretion drainage for prevention of ventilation associated pneumonia]. Zhongguo Wei Zhong Bing Ji Jiu Yi Xue Chin Crit Care Med Zhongguo Weizhongbing Jijiuyixue. 2008 Jun;20(6):338–40.

35. Kollef MH, Skubas NJ, Sundt TM. A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. Chest. 1999 Nov;116(5):1339–46.

36. Smulders K, Van der Hoeven H, Weers-Pothoff I, Vandenbroucke-Grauls C. A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. CHEST J. 2002;121(3):858–62.

37. Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. Crit Care Med. 2011;39:1985–91.

38. Dezfulian C, Shojania K, Collard HR, Kim HM, Matthay MA, Saint S. Subglottic secretion drainage for preventing ventilator-associated pneumonia: a meta-analysis. Am J Med. 2005 Jan;118(1):11–8.

39. Fernandez JF. Technologic Advances in Endotracheal Tubes for Prevention of Ventilator-Associated Pneumonia. CHEST J. 2012 Jul 1;142(1):231.

40. Park DR. Antimicrobial treatment of ventilator-associated pneumonia. Respir Care. 2005;50(7):932–55.

Appendix

section:1

Data collection sheet used in our study: page 1

INCIDENCE OF VAP/VAEs ETT-SS (VS) ETT-C IN SICU/AICU

S.NO-

PATIENT NAME: AGE: M/F

BRADMA

HOSPITAL NUMBER:

DURATION OF VENTILATION >48HRS: Y/N

DATE & TIME OF ICU ADMISSION:

PRIMARY DIAGNOSIS:

CHRONIC ILLNES:

APACHE II SCORE:

TYPE OF ENDOTRACHEAL TUBE: ETT-SS /ETT-C

TIME AND DATE OF EXTUBATION:

MORTALITY IN ICU/WARD:

DATE &TIME OF ICU DISCHARGE:

DATE OF HOSPITAL DISCHARGE:

REINTUBATION DETAILS IF ANY :

Data collection sheet used in our study:page 2

MV Day	PEEP min	MAP min	FiO2 min	TEMP min	TEMP max	WBC count	ANTIBIOTICS	SPECIMEN TYPE	PURULENT SECRETION +/-	POLYMORPHS/ EPIS	ORGANISM(S)	VAE +/_

APRV MODE: MENTION AS **APRV** IN PEEP COLUMN

PEEP min- The lowest value of PEEP during a calendar day that is set on the ventilator and *maintained for at least 1 hour.*

FIO2 min - The lowest value of FiO2 during a calendar day that is set on the ventilator and *maintained for at least 1 hour*.

MAP min - The lowest value of Mean Airway Pressure during a calendar day that is set on the ventilator and *maintained for at least 1 hour.*

section:2

PATIENT INFORMATION SHEET

A PROSPECTIVE OBSERVATIONAL STUDY COMPARING THE EFFECT OF ENDOTRACHEAL TUBE WITH SUBGLOTTIC SUCTION PORT VS STANDARD ENDOTRACHEAL TUBE ON INCIDENCE OF VENTILATOR ASSOCIATED PNEUMONIA IN PATIENTS VENTILATED FOR >48 HRS IN ICU

This study, in which your relative is being asked to participate, is being conducted to assess the effectiveness of Endo-tracheal tube with subglottic suction port (ETT SS) in reducing pneumonia associated with ventilation.

As part of the study, data will be collected from medical records.

Your relative will not have to undergo any special investigations in this study.

This consent is for collecting some important details with regard to your relative such as,

1. Type of Endotracheal tube used for intubation (the plastic tube used to give breaths from the ventilator or breathing machine),

2. Number of days on the ventilator (breathing machine) and ventilator settings,

3. Details regarding ICU & hospital stay,

4. Details regarding the germ growth from your lung secretions (Endotracheal Aspirate microbiology culture report),

5. Details regarding your relatives long term or previously known illness and reason for the admission into the ICU,

These details are collected for a research to find whether any significant advantage(s) is /are present in the use of ETT SS –Endotrachel Tube with subglottic suction port (this port allows periodical clearance of saliva which pools above the cuff which seals it around the windpipe) in comparison with ETT C-standard Endotracheal tube without suction port .

The main purpose of this research is to find out whether the ETT SS usage offers considerable advantage in prevention of VAP- Ventilator Associated Pneumonia (a disease associated with the saliva dribbling past the breathing tube into the wind pipe resulting in lung infection).

As the results are just observed we will not interfere in any of the decisions made by ICU doctors regarding treatment, laboratory investigations etc.

I understand that my relative will not be offered any financial benefits because of participation in this study

The study details will be kept confidential in terms of personal information received from patients. Only the end results of the study will be published. The primary data collected will be kept with the primary investigator.

Consenting to be part of the study is purely voluntary. You can withdraw from the study at any time and no explanation needs to be offered regarding the same.

The further course of treatment will follow the standard protocol and in no way you will be penalized for it.

Your relative is eligible for the standard care offered to all patients in CMC, Vellore. None of the study patients will be deprived of the available therapies.

Any new information regarding the findings, if significant, will be notified to you.

In the event of any further queries about the study, risks and benefits at any point of the study, you can contact Dr. Sivakumar.G 0416 – 2282105 / 9842318899.

Primary investigator-

Dr. Sivakumar. G,

Senior Resident,

Dept of Anesthesiology,

Christian Medical College -Vellore.

Ph. No.9842318899, 04162282105.

Email : sivadoc@gmail.com

section:3

INFORMED CONSENT FORM :

1) *Study Title:* ***A Prospective Observational Study comparing the effect of Endotracheal Tube with Subglottic Suction Port vs standard Endotracheal tube on Incidence of Ventilator associated Pneumonia in patients ventilated for > 48 hrs in ICU.***

Patient's Name: _____

Date of Birth / Age: _____

Relatives name & Initials: _____

*Relationship:*_____

Please mark in the boxes after reading,

(i) I confirm that I have read and understood the information sheet dated _____for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my relative's participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my/his/her medical care or legal rights being affected. [ ]

(iii) I understand that the cost of treatment and surgery I my relative is being charged is identical to other patients not participating in this study. I am aware that my relative will not be offered any monetary / other benefits.

(iv) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. [ ]

(v) I understand that my relatives identity will not be revealed in any information released to third parties or published. [ ]

(vi) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(vii) I assent my relative to take part in the above study. [ ]

Signature (or Thumb impression) of the Legally Acceptable Representative

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

For Any Further clarifications contact: Dr. Sivakumar.G at 0416 –2282105 / 9842318899.email:sivadoc@gmail.com.

Section:4

List of Antimicrobial Agents Eligible for IVAC, Possible and Probable VAP

Antimicrobial Agent :

- AMIKACIN
- AMPHOTERICIN B
- AMPHOTERICIN B LIPOSOMAL
- AMPICILLIN
- AMPICILLIN/SULBACTAM
- ANIDULAFUNGIN
- AZITHROMYCIN
- AZTREONAM
- CASPOFUNGIN
- CEFAZOLIN
- CEFEPIME
- CEFOTAXIME
- CEFOTETAN
- CEFOXITIN
- CEFTAROLINE
- CEFTAZIDIME
- CEFTIZOXIME
- CEFTRIAXONE
- CEFUROXIME
- CIPROFLOXACIN
- CLARITHROMYCIN
- CLINDAMYCIN
- COLISTIMETHATE
- DORIPENEM
- DOXYCYCLINE
- ERTAPENEM
- FLUCONAZOLE
- FOSFOMYCIN
- GEMIFLOXACIN
- GENTAMICIN
- IMIPENEM/CILASTATIN
- ITRACONAZOLE

- LEVOFLOXACIN
- LINEZOLID
- MEROPENEM
- METRONIDAZOLE
- MICAFUNGIN
- MINOCYCLINE
- MOXIFLOXACIN
- NAFCILLIN
- OSELTAMIVIR
- OXACILLIN
- PENICILLIN G
- PIPERACILLIN
- PIPERACILLIN/TAZOBACTAM
- POLYMYXIN B
- POSACONAZOLE
- QUINUPRISTIN/DALFOPRISTIN
- RIFAMPIN
- SULFAMETHOXAZOLE/TRIMETHOPRIM
- SULFISOXAZOLE
- TELAVANCIN
- TELITHROMYCIN
- TETRACYCLINE
- TICARCILLIN/CLAVULANATE
- TIGECYCLINE
- TOBRAMYCIN
- VANCOMYIN, intravenous only
- VORICONAZOLE
- ZANAMIVIR

Section : 5 PATIENT DATA

uid	hospno	hospno1	age	sex	health	dm	htn	ihd	cld	crf	vhd	tb	af	thyroid	copd
1	901552	F	24	1	13	0	0	0	0	0	0	0	0	0	0
2	901313	F	44	0	21	1	1	1	0	0	0	0	0	0	0
3	806099	F	49	0	13	0	0	0	0	0	0	0	0	0	0
4	817108	F	21	0	22	0	0	0	0	1	0	0	0	0	0
5	775259	F	67	1	33	1	1	0	1	0	0	0	0	0	0
6	862826	F	41	1	33	0	0	0	0	0	0	0	0	0	0
7	380000	F	28	1	22	1	0	0	0	0	0	1	0	0	0
8	630929	F	51	1	25	0	0	0	0	0	0	0	0	0	0
9	904980	F	52	1	26	0	0	0	0	0	0	1	0	0	0
10	904980	F	52	1	25	0	0	0	0	0	0	1	0	0	0
11	907795	F	41	1	33	1	1	0	0	0	0	0	0	0	0
12	912833	F	60	1	29	0	0	0	0	0	0	0	0	0	0
13	910033	F	62	1	42	0	0	0	0	0	0	0	0	0	0
14	909563	F	35	1	17	0	0	0	0	0	0	0	0	0	0
15	907439	F	48	1	69	1	0	0	0	0	0	0	0	0	0
16	1468	G	50	1	13	0	0	0	0	0	0	0	0	0	0
17	896121	C	58	1	41	1	1	1	0	0	0	0	0	0	0
18	914553	F	64	1	25	1	1	1	0	0	0	0	1	0	0
19	849827	C	65	1	28	0	1	1	0	0	0	0	0	0	0
20	832879	F	67	1	25	0	1	0	0	0	0	0	0	0	0
21	909925	F	34	1	29	0	0	0	0	0	0	0	0	0	0
22	907134	F	35	1	5	0	0	0	0	0	0	0	0	0	0
23	313898	F	56	0	27	1	1	0	0	0	0	0	0	0	0
24	915985	F	70	1	13	0	1	0	0	0	0	0	0	0	0
25	902588	F	65	1	28	1	0	0	0	0	0	0	0	0	0
26	902465	F	24	1	23	0	0	0	0	0	0	0	0	0	0
27	902649	F	16	1	17	0	0	0	0	0	0	0	0	0	0
28	901446	F	51	1	12	1	0	0	0	0	0	0	0	0	0
29	901969	F	57	1	35	0	0	0	0	0	0	0	0	0	0
30	830848	F	45	1	11	0	0	0	0	0	0	0	0	0	0
31	909937	F	61	1	22	0	0	0	0	0	0	0	0	0	0
32	909360	F	38	0	22	0	0	0	0	0	0	0	0	0	0
33	910279	F	42	1	22	0	0	0	0	0	0	0	0	0	0
34	851149	F	34	0	27	0	0	0	0	0	0	0	0	0	0
35	856491	F	55	1	25	0	0	0	0	0	0	0	0	0	0
36	912961	F	23	1	18	0	0	0	0	0	0	0	0	0	0
37	904270	F	37	1	15	0	0	0	0	0	0	0	0	0	0
38	904322	F	71	0	42	1	0	1	0	1	0	0	0	0	0
39	914866	F	33	1	34	0	0	0	0	0	0	0	0	0	0
40	915012	F	55	1	11	0	0	0	0	0	0	0	0	0	0
41	917717	F	31	1	42	0	0	0	0	0	0	0	0	0	0
42	910369	F	51	1	12	1	1	0	0	1	0	0	0	0	0
43	909360	F	37	0	22	0	0	0	0	0	0	0	0	0	0
44	807286	F	40	1	19	0	1	0	0	0	0	0	0	0	0
45	804540	F	55	0	33	1	0	0	0	0	0	0	0	0	0
46	901588	F	44	1	32	1	0	0	0	1	0	0	0	0	0
47	685072	F	51	1	32	0	0	0	0	1	0	0	0	0	0
48	912912	F	40	1	21	0	1	0	0	0	0	0	0	0	0
49	914207	F	28	0	20	0	0	0	0	0	0	0	0	0	0
50	907645	F	30	1	13	0	0	0	0	0	0	0	0	0	0
51	910181	F	45	1	17	0	0	0	0	0	0	0	0	0	0
52	910288	F	37	1	15	1	0	0	0	0	0	0	0	0	0
53	912469	F	19	0	12	0	0	0	0	0	0	0	0	0	0
54	907038	F	46	1	13	0	0	0	0	0	0	0	0	0	0
55	855486	F	38	1	9	0	0	0	0	0	0	0	0	0	0
56	912529	F	19	1	17	0	0	0	0	0	0	1	0	0	0
57	910567	F	34	1	24	0	0	0	0	0	0	0	0	0	0
58	904413	F	55	1	21	0	0	0	0	0	0	0	0	0	0
59	914252	F	40	1	20	0	0	0	0	0	0	0	0	0	0
60	907696	F	19	0	27	0	0	0	0	0	0	0	0	0	0
61	907251	F	62	1	32	0	0	0	0	0	0	0	0	0	0
62	822326	F	56	1	22	1	0	0	0	0	0	0	0	1	0
63	54521	F	38	1	20	0	0	0	0	0	0	0	0	0	0
64	199946	F	46	1	32	0	0	0	0	1	0	0	0	0	0
65	910008	F	54	0	32	1	0	0	0	0	0	0	0	0	0
66	796086	F	62	0	19	0	0	0	0	0	0	0	0	1	0
67	3373	G	32	0	18	0	0	0	0	0	0	0	0	0	0
68	597438	D	69	0	36	1	1	1	0	0	0	0	0	0	0
69	914120	F	60	1	38	1	1	1	0	0	0	0	0	0	0

70	876557	F	58	1	19	0	0	0	0	0	0	0	0	0	0
71	720041	F	61	0	34	1	1	0	0	0	0	0	0	0	0
72	759709	F	53	1	28	0	0	0	0	0	0	0	0	0	0
73	431483	D	42	1	32	0	0	0	0	0	0	0	0	0	0
74	817163	F	28	1	11	0	0	0	0	0	0	0	0	0	0
75	915595	F	42	1	10	0	0	0	0	0	0	0	1	0	0
76	902192	F	20	1	18	0	0	0	0	0	0	0	0	0	0
77	917506	F	60	0	31	1	0	0	0	0	0	0	0	0	0
78	758447	F	19	0	28	0	1	0	0	0	0	0	0	0	0
79	77559	F	41	1	41	1	0	0	1	1	0	0	0	0	0
80	920373	F	53	0	27	1	0	0	0	0	0	0	0	0	0
81	920906	F	46	1	17	0	0	0	0	0	0	0	0	0	1
82	915676	F	16	0	26	0	0	0	0	0	0	0	0	0	0
83	8027		81	1	16	1	1	1	0	0	0	0	0	0	1
84	912203	F	19	0	15	0	0	0	0	0	0	0	0	0	0
85	920428	F	78	1	26	1	1	1	0	0	0	0	0	0	1
86	920433	F	32	1	21	0	0	0	0	0	0	0	0	0	0
87	920767	F	40	0	13	0	0	0	0	0	0	0	0	0	0
88	916747	F	20	0	31	0	0	0	0	0	0	0	0	0	0

diag	ett	vae	mvdays	icustay	hospstay	dama	hospmort
TRAUMA BLUNT ABDOMEN # FEMUR TIBIA	1	0	5	5	19	0	0
NECROTISINS FASCITIS R LEG	1	0	3	3	11	0	0
POST OP EXCISION CA TONGUE	1	0	3	3	10	0	0
UROSEPSIS POST OP CYSTOPLASTY	1	0	7	7	9	0	0
AML FEBRILE NEUTROPENIA	0	0	4	4	4	0	1
ALL KLEBSIELLA SEPSIS	0	1	10	10	10	0	1
DISSEMINATED T.B IATROGENIC CUSHING	0	0	14	14	14	0	1
POST OP ENTEROTOMY POST HARTMAN REVERSAL	0	0	7	8	20	0	0
INTESTINAL LYMPHOMA ILEAL PERFORATION	0	0	6	6	17	0	1
SATUS POST OP ILEL PERFORATION CLOSURE, ACUTE MI	0	0	15	15	17	0	1
ENTERO-CUTANEOUS FISTULA POSTOP GASTROSTOMY	0	1	26	34	40	0	0
ISCHIORECTAL ABCESS ABD WALL NECROTISING FASCITIS	0	0	3	3	3	1	0
LEFT FOOT GANGRENE POSTOP B.K AMPUTATION	0	0	3	3	3	1	0
SMALL BOWEL GANGRENE POSTOP RESECTION ANASTAMOSIS	0	0	6	6	17	0	0
TRAUMA LIVER LACERATION R EYE LACERATION # R ANKLE R ORBIT	0	0	7	8	14	0	0
CA TONGUE POSTOP HEMIGLOSSECTOMY RADIAL FREE FLAP MRND	1	0	2	2	7	0	0
NECROTISING FASCITIS R FOOT SEPTIC SHOCK ARF	0	0	2	2	2	0	1
SMALL BOWEL GANGRENE	1	0	3	4	12	0	0
ACUTE CHOLECYSTITIS	0	0	4	6	10	0	0
PLASMABLASTIC LYMPHOMA SEPTIC SHOCK	0	0	6	6	6	0	1
TRAUMA LEFT THIGH CRUSH INJURY L FEMUR#	1	0	3	3	3	0	1
STAB INJURT LIVER LACERATION HEMO PERICARDIUM	1	0	3	4	6	0	0
LEFT LEG CELLULITIS	1	0	2	3	12	0	0
CELLULITIS R LOWER LIMB	0	0	4	7	20	0	0
FOURNIERS GANGRENE	0	0	4	4	21	0	0
TRAUMA #S B/L FEMUR R ULNA R RADIUS	1	0	5	5	10	0	0
TRAUMA #S L FEMUR,ACETABULLAM,HUMERUS,STABLE # C1 VERTEBRA	1	0	3	4	15	0	0
TRAUMA #S R ZYGOMA R CLAVICLE R FEMUR R TIBIA	1	0	3	4	12	0	0
TRAUMA BLUNT ABDOMEN	1	0	3	3	3	1	0
CA TONGUE POSTOP WLE MRND FREE FLAP	1	0	4	2	2	0	0
BULL GORE PENETRATING ABDOMINAL INJURY	1	0	3	5	13	0	0
TRAUMA # R TIBIA WET GANGRENE POSTOP R AK AMPUTATION	1	0	2	2	2	0	1
TRAUMA RTA OPEN PELVIS # ,RECTAL & BLADDER INJURY, L HIP #	1	4	10	10	10	0	1
CA RECTUM POSTOP LAR ANASTAMOTIC LEAK	0	0	2	2	2	0	1

PERFORATED CA CAECUM	1	4	6	7	8	0	0
RTA POLY-TRAUMAB#S R FEMUR R TIBIA & R FOREARM INJURY	1	0	2	3	12	0	0
RTA # R TIBIA, HEAD INJURY	0	0	5	6	22	0	0
R GLUTEAL ABCESS ARF	1	0	2	2	2	1	0
ACUTE SEVERE PANCREATITIS	0	1	27	27	27	0	1
TRAUMA #S R PATELLA,L OLECRANON, L TIBIA	0	0	10	11	22	0	0
TRAUMA # R FEMUR	1	0	2	4	8	0	0
R FOOT CELLULITIS	0	0	3	3	15	0	0
TRAUMA R TIBI # WET GANGRENE	1	0	2	2	2	0	1
AML MASSIVE UGI BLEEDING ,FEBRILE NEUTROPENIA	0	0	4	4	4	0	1
NON HEALING BEDSORE NECROTISING FASCITIS ANT ABDOMINAL WALL	0	0	5	5	5	0	1
MUCORMYCOSIS L MAXILLARY SINUS,L ORBIT	1	0	5	5	5	0	1
RELAPSED MULTIPLE MYELOMA	0	0	4	6	14	0	0
RTA BLUNT ABD TRAUMA,L1-L4 TRANSVERSE PROCESS #,RIB #	1	0	2	6	10	0	0
BLUNT TRAUMA ABD,LIVER LACERATION,KIDNEY INJURY	0	0	3	5	12	0	0
RTA L FEMUR #,FEMORAL ARTEY INJURY	0	0	3	3	24	0	0
RTA MANGLED R LOWER EXTREMITY	1	0	3	3	3	1	0
RTA # R RADIUS ,L FEMUR,L FIBULA & L OPEN KNEE	1	0	4	5	12	0	0
RTA CRUSH INJ L LOWER LIMB,R FEMUR #,BLUNT ABD TRAUMA	1	0	2	2	20	0	0
RTA POLYTRAUMA LEFT LEG BB#,JEJUNAL PERFORATION,L RIBS #	1	0	5	6	12	0	0
CA TONGUE WLE	1	0	2	2	8	0	0
ABDOMINAL TB,HOLLOW VISCUS PERFORATION	1	0	6	6	6	0	1
POLYTRAUMA #D5,# FEMUR,BLUNT TRAUMA ABD,JEJUNAL PERFORATION	1	0	5	5	28	0	0
RTA BLUNT ABD TRAUMA,B/L RIB #S	1	0	4	10	14	0	0
PRE PYLORIC PERFORATION	1	0	4	4	13	0	0
POST OP LSCS PRES	1	0	2	3	8	0	0
L THIGH CELLULITIS	1	0	8	9	26	0	0
CH PYELONEPHRITIS,PROSTATITIS,POSTOP TURP NEPHRECTOMY	1	0	2	2	6	0	0
RTA -R THIGH INJURY,HEAD INJURY -FOCAL HAMORRHAGE	1	0	3	4	13	0	0
B/L RENAL CALCULI OBSTRUCTIVE UROPATHY	1	0	6	6	8	0	0
L LEG NECROTISING FASCITIS	1	2	6	6	6	0	1
CHOLANGIO CARCINOMA POST OP HEPATECTOMY+HEP-JEJUNOSTOMY	1	0	2	5	22	0	0
CA RECTUM & OVARY,POST OP ANASTAMOTIC LEAK	1	0	3	3	10	0	0
ILEAL GANGRENE,ADHESIVE BANDS	1	0	8	8	14	0	1
R LOWER LIMB NECROTISING SOFT TISSUE INFECTION	0	0	15	15	15	0	1

APPENDICIAL MUCOSAL NEOPLASM,ILEOCECAL INTUSUSSEPTION	0	0	13	13	13	0	1
PAOD L FOOT GANGRENE	0	0	4	4	4	1	0
MYELODYSPLASTIC SYNDROME	0	0	4	4	4	0	1
R LEG NECROTISING FASCITIS	0	0	2	4	15	0	0
VENOUS MALFPRMATION L CHEEK /TONGUE	1	0	2	3	6	0	0
R LEG NECROTISING SOFT TISSUE INFECTION	0	1	7	7	7	0	1
RTA # R TIBIA	0	0	5	5	9	0	0
NECROTISING INFECTION ANT ABD WALL,PERINEUM,L THIGH	0	0	3	3	3	0	0
SEV PRE ECCLAMPSIA,POST PARTUM SEPSIS	0	0	7	8	23	0	0
L LEG NECROTISING SOFT TISSUE INFECTION	0	0	4	5	12	0	0
LEFT LEG CELLULITIS	0	2	13	13	13	1	0
SMALL BOWEL ISCHEMIA POST OP RESCTION ANASTAMOSIS	0	0	3	3	3	1	0
SMALL BOWEL OBSTRUCTION,POST OP ADHESIOLYSIS	0	0	7	7	7	0	1
CHOLEDOCHOLITHIASIS CHRONIC PANCREATITIS	0	0	4	4	14	0	0
TRAUMA BLUNT ABD-JEJUNAL PERFORATION,# TRANV PROCESS L2L3L4	0	0	11	12	15	0	0
NECROTISING FASCITIS L HAND FOREARM POSTOP DEBRIDEMENT	0	0	4	5	14	0	0
RTA # ACETABULLAM,PELVIC RAMUS,R RENAL INJURY	1	0	6	7	20	0	0
RTA BLUNT ABD TRAUMA,LIVER LACERATION	0	0	4	4	21	0	0
PRIMI POST OP LSCS ?VIRAL MYOCARDITIS	1	0	7	10	27	0	0